GEORGIA INSTITUTE OF TECHNOLOGY OFFICE OF CONTRACT ADMINISTRATION

PROJECT ADMINISTRATION DATA SHEET

[x] ORIGINAL

[ ] REVISION NO. ____

Project No. E-19-654 DATE: 6/5/81

Project Director: Dr. A. P. Yoganathan School/~~Lab~~ Chemical Engineering

Sponsor: DHHS/PHS; Food and Drug Administration; Rockville, MD 20857 x/1+

Type Agreement: Contract #223-81-5000 ~~5/3/82~~ 6/28/83

Award Period: From 6/1/81 To ~~7/31/82~~ (Performance) — (Reports)

Sponsor Amount: $69,855 Contracted through:

Cost Sharing: $10,000 (E-19-359) GTRI/~~GIT~~

Title: Prosthetic Heart Valves: A Study of In Vitro Performance

ADMINISTRATIVE DATA OCA CONTACT DUANE HUTCHISON x4820

1) Sponsor Technical Contact: Dr. William G. Letzing, Project Officer; Department of Health and Human Services; Public Health Service; Food and Drug Administration; HFA-512; 5600 Fishers Lane, Room 12A-17; Rockville, MD 20857

2) Sponsor Admin./Contractual Contact: ~~A. Christine Manuel~~ Ms. Molly SHCD, Contract Administrator; Department of Health and Human Services; Public Health Service; Food and Drug Administration, HFA-512; 5600 Fishers Lane, Room 12A-17; Rockville, Maryland 20857

Reports: See Deliverable Schedule Security Classification: none

Defense Priority Rating: none

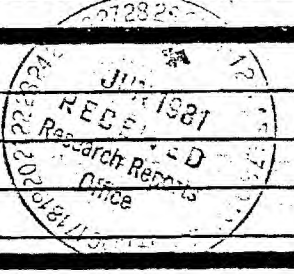
RESTRICTIONS

See Attached Government Supplemental Information Sheet for Additional Requirements

Travel: Foreign travel must have prior approval - Contact OCA in each case. Domestic travel requires sponsor approval where total will exceed greater of $500 or 125% of approved proposal budget category.

Equipment: Title vests with Government, except that items costing less than $1,000 vests with GIT if prior approval to purchase is obtained from the Contracting Officer.

COMMENTS:



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GEORGIA INSTITUTE OF TECHNOLOGY OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION/CLOSEOUT SHEET

Date January 17, 1984

Project No. E-19-654 School/~~Dept~~ ChE

Includes Subproject No.(s)

Project Director(s) Dr. A. P. Yoganathan GTRI / ~~GTL~~

Sponsor DHHS/PHS; Food and Drug Administration; Rockville, MD 20857

Title "Prosthetic Heart Valves: A Study of In Vitro Performance"

Effective Completion Date: 6/28/83 (Performance) 11/30/83* (Reports)

Grant/Contract Closeout Actions Remaining:

- [ ] None
- [ ] Final Invoice or Final Fiscal Report
- [ ] Closing Documents
- [X] Final Report of Inventions
- [X] Govt. Property Inventory & Related Certificate
- [ ] Classified Material Certificate
- [ ] Other

*The reporting period extension was not formally approved, however, verbal approval was given to use remaining funds for report preparation as necessary.

Continues Project No. Continued by Project No.

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Form OCA 60:1028

ABSTRACT

In order to identify and define the fluid dynamic characteristics of primary importance in quantifying heart valve performance, GTRI has carried out a paper study of this subject under contract with the FDA. Where possible these fluid dynamic characteristics have been related to valve hemodynamics and clinical complications such as hemolysis, thromembolism, thrombus formation, tissue overgrowth and other valve dysfunctions.

This Phase I study is intended to provide a better understanding for the need to establish *in vitro* flow testing guidelines which encompass state-of-the-art instrumentation and methodology. The study indicates very clearly that there is more to the *in vitro* and *in vivo* fluid dynamic performance of a heart valve prosthesis other than pressure drop and regurgitation. The study also indicates the need for good clinical follow up data on heart valve recipients, analysis of sub-lethal and/or lethal damage to blood components and endothelial tissue, and detailed pathologic studies on recovered (at surgery and/or autopsy) valve prostheses.

III. CONCLUSIONS

Following the collection, analysis, and interpretation of the in vivo and in vitro information and data pertaining to the current state of the art in respect to the safety and performance of prosthetic heart valves (mechanical and tissue), Georgia Tech concludes that:

(1) At present we do not have an ideal prosthetic heart valve. During the past 20 years manufacturers have developed and produced various designs of prosthetic heart valves, some of which perform satisfactorily when implanted surgically in patients suffering from valvular heart disease. Other designs have had to be removed from the open market due to lack of adequate safety and efficiency.

(2) There is a lack of in vivo clinical and in vitro fluid dynamic data and information on all designs of prosthetic heart valves in current clinical use. The lack of good quality clinical information and data on some of the older valve types is surprising.

(3) Good long term clinical follow up data exists only for the following valves types studied: (i) Starr-Edwards ball valves, (ii) Bjork-Shiley tilting disc valve, (iii) Lillehei-Kaster tilting disc valve, and (iv) Hancock porcine valve.

(4) There is a lack of good detailed pathologic studies performed on heart valves recovered at surgery and/or autopsy. The lack of such studies will hinder the progress and development of not only better heart valve prostheses but also other future artificial devices such as left ventricular assist devices and the total artificial heart.

(5) The caliber and quantitative nature of the in vitro fluid dynamic studies has improved a great deal during the past five to six years. There are, however, many pieces of information missing which would give us a better understanding of

some of the clinical problems observed with prosthetic heart valves.

(6) There seems to be a lack of collaboration between the in vitro investigator and the physician (cardiologist and/or cardiovascular surgeon). Therefore, there are very few articles that attempt to relate specific in vitro flow characteristics to clinical performance and complications. The lack of such information will impede the progress of prosthetic heart valves and similar cardiovascular devices.

(7) The available in vivo hemodynamic and in vitro pressure drop results from all valves when analyzed in a combined overall manner indicate that the prostheses studied could be arranged in the following order of decreasing stenoticity: (i) caged disc valves designs; (ii) caged ball valves, Lillehei-Kaster tilting disc valve and porcine valves; (iii) Bjork-Shiley tilting disc valve and Ionescu-Shiley pericardial valve; (iv) Hall-Kaster tilting disc valve; (v) St. Jude bi-leaflet valve.

(8) In terms of regurgitation, in vitro studies indicate that the values can be arranged in the following order increasing regurgitation: (i) porcine valves; (ii) Ionescu-Shiley pericardial valve; (iii) Starr-Edwards and Braunwald-Cutter ball valves, and Kay-Shiley and Beall disc valves; (iv) Smeloff-Cutter ball valve, Bjork-Shiley, Lillehei-Kaster, Hall-Kaster tilting disc valves, and St. Jude bi-leaflet valve.

(9) All prosthetic valves (mechanical and tissue) in current clinical use cause sub-lethal and/or lethal damage to blood elements such as red cells and platelets. The shear fields created by the valves are all capable of causing such damage. Sub-lethal damage to red cells could in time lead to mild hemolysis. Similarly, sub-lethal damage to platelets could over a period of time lead to thromboemboli and complications.

(10) All peripheral flow type valves cause damage to the endothelial lining of the proximal ascending aorta. This is directly related to the elevated wall shear stresses in the immediate downstream vicinity of these valves. They may also cause sub-lethal and/or lethal damage to the ventricular wall. Other mechanical designs and tissue bioprostheses could cause sub-lethal and/or lethal damage to the endothelial lining of the aortic wall. The jet type flow from the tissue valves could cause damage to the ventricular wall. Depending on the orientation of the valve the flow in the major orifice region of the tilting disc valve could also cause damage to the ventricular wall.

(11) All prosthetic valves in current clinical use cause hemolysis and thromboembolic complications and are prone to the problems of thrombus formation and excess tissue growth on the valve superstructure.

(12) In many cases the hemolysis caused by the prosthesis is mild or moderate and is generally compensated for quite adequately by the bone-marrow. Cloth covering on the valve superstructure (such as with the Starr-Edwards and Beall valves) will lead to an increase in hemolysis depending on the structure and surface characteristics of the fabric. Hemolysis, however, mild is <u>not</u> innocuous. It is the forerunner in one of the proposed mechanisms for platelet aggregation and coagulation which could lead to the formation of thromboemboli.

(13) Mechanical valves in current clinical use have TEC rates of about 2 to 8% per pt yr for patients on anticoagulation therapy. Tissue valves have TEC rates of about 2 to 5.5% per pt yr without long term anticoagulation therapy.

(14) Thrombus formation and tissue overgrowth on the valve superstructure are most often found in regions of flow stasis, very low flow and shear, and flow separation.

(15) Mechanical damage to the blood elements as well as to the endothelial tissue of the adjacent vessel wall, may in addition trigger complex biochemical reactions which could lead to the excess fibrous tissue overgrowth observed on recovered valves.

(16) Tissue valves are prone to calcification especially in children. Calcification mainly occurs on the outflow surface of the leaflet. Therefore, it is very probable that the relatively stiff nature of the current leaflets, together with the region flow separation between outflow surface of the leaflets and vessel wall, could lead to the deposition of thrombotic and calcific material on the leaflets.

IV. RECOMMENDATIONS

1. Set up a national registry for prosthetic heart valves immediately. Detailed pathologic, and non-destructive and destructive engineering studies should be conducted on recovered valves, under the auspicies of the registry. At the time of valve implantation surgery, patients should be requested to sign a release so that the valve or valves may be recovered for scientific purposes at death. Current implant retrieval programs conducted by some of the manufacturers do not facilitate free transfer of information among the medical and scientific communities. It seems as if those valve prostheses disappear from the public domain.
2. An educational program should be established for patients which provides reliable and accurate scientific information regarding the current status of various heart valve prostheses, their uses and limitations, and potential problems.
3. Require good clinical follow up data on all designs of valve prostheses. Such clinical follow up should include more detailed and sensitive tests to study blood component damage. For example, half-life studies should be conducted on tagged red cells and platelets. The filterability of the red cells in micropores should also be studied. It may be necessary in the initial stages to sponsor such studies at a few major medical centers.
4. Standardized methodology should be established for reporting hemodynamic, hemolysis and TEC data. Such an effort would require the cooperation of the American Heart Association, American College of Cardiology and American Association of Thoracic Surgeons.
5. Guidelines for the *in vitro* fluid dynamic testing of heart valves should be set up immediately. Such guidelines should include not only pressure drop,

regurgitation and flow visualization studies, but also velocity and shear stress measurements in the immediate vicinity of the valve. Such measurements are necessary to understand the clinically observed problems of hemolysis, thromboembolism, thrombus formation, excess tissue overgrowth and damage to the endothelial lining of vessel walls. Fluid dynamic studies should be conducted under steady and pulsatile flow conditions.

6. An inter-laboratory comparison program for new and recovered heart valve prostheses should be established, under the auspicies of the Bureau of Medical Devices Laboratory.
7. A task by task program for the fluid dynamic evaluation of prosthetic heart valves in current clinical use should be established. Such studies should be jointly supported by manufacturers and the FDA.
8. Further studies should be conducted to elucidate the answers to the problems of sub-lethal and/or lethal damage to all blood elements and endothelial tissue.
9. A national or international conference on prosthetic heart valves should be held within the next year or two. The last such conference was held in 1969. The conference participants should include cardiovascular surgeons, cardiologists, cardiovascular pathologists, manufacturers and BMD personnel.
10. Improve communication between the physicians (cardiologists and cardiovascular surgeons) and engineers. The medical community should understand the value of <u>in vitro</u> testing and the problems associated with such testing studies. On the other hand the engineer should understand the problems faced by the cardiovascular surgeon and cardiologist. The communication should take place in both directions.

PROSTHETIC HEART VALVES: A STUDY OF *IN VITRO* PERFORMANCE

LETTER REPORT (6/1/81 - 6/30/81)

The FDA contract on the *in vitro* flow characteristics of prosthetic heart valves officially started on 6/1. Due to spring quarter examinations, graduation and quarter break, actual work on Phase I of the project did not start until 6/22. We have since then, run a complete and thorough computerized literature search on prosthetic heart-valve performance. The search which includes both medical and engineering literature dates back to about 1967. In addition, we have contacted the major valve manufacturers (Edwards, Shiley etc.) to provide any articles they may have. We are presently in the process of xeroxing important articles (identified from the computer search) both at Georgia Tech and the Emory University Medical school. Professor Yoganathan and Dr. Harrison met for two days (June 26 & 27) in Los Angeles. They discussed material that could be used for Phase I.

The following prosthetic heart valves will be studied in Phase I: Starr-Edwards (ball valve), Bjork-Shiley, Kay-Shiley, Beall, Smeloff-Cutter, Braunwald-Cutter, Lille hei-Kaster, Hall-Kaster, Hancock, Carpentier-Edwards, Ionescu-Shiley, St. Jude, and Angell-Shiley.

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

LETTER REPORT (7/1/81-7/31/81)

Work on phase I of the project started in earnst. Articles on the different valves mentioned in last months letter report are being read and analyzed. We have during the past month concentrated on the medical (surgical and clinical) literature. Articles that pertain to large groups of valve recepients are being favored. Books on heart valve prostheses are also being studied. The scientific documentation of the medical articles leaves much to be desired, and we are doing our very best to extract as much quantitative and relevent qualitative data as possible. Well documented in vivo hemodynamic data on normally functioning prosthetic valves has been collected and is being tabulated. The amount of such data available varies tremendously from one valve type to the next. There seems to be a fair amount of data on the St. Jude and Hall-Kaster valves due to FDA regulations. For some of the older valve types very little good data exists. Once again documentation is sketchy.

One of the most obvious areas where there is a tremendous lack of information is on the pathology of recovered (surgery or autopsy) heart valves and their respective hearts. At the present time only Dr. W. C. Roberts (NIH) has well documented pathology studies in the open literature. One of our medical consultants (Dr. Earl C. Harrison) has studied a large number of recovered heart valves. He has an extensive photographic library of these recovered valves. He has, however, not published detailed pathologic studies on his valve collection, due to the lack of financial resources and time. It is apparent to us, that there is presently no incentive at major valve centers to conduct detailed pathologic studies on recovered prosthetic vlaves. Therefore it is our opinion that a national center or centers be established immediately to study recovered prosthetic heart valves and related cardiovascular devices.

When we complete our study of the medical literature, we will then turn our attention to the engineering literature for in vitro data on the various prosthetic heart valves.

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

LETTER REPORT (9/1/81-10/31/81)

During the month of September the draft report for Phase I was completed and mailed to the sponsor. We are presently awaiting the technical review of the draft report.

Phase II of the project was started on 9/1/81. In the experimental program we are studying the following valves: (1) Starr-Edwards-1260, (2) Starr-Edwards 6120, (3) Bjork-Shiley (convexo-concave), (4) St. Jude, (5) Beall, (6) Smeloff-Sutter, (7) Ionescu-Shiley, (8) Carpentier-Edwards, (9) Hancock (standard) and (10) Hancock (modified orifice). It is proposed to add the Hall-Kaster aortic and mitral valves to study later on depending on the availability of time.

Steady flow pressure drop studies are currently in progress, while the flow visualization studies were completed as planned at the end of September. As reported in our letter of October 19, the only problems with valves purchased under the contract pertain to the Carpentier-Edwards and Hancock porcine valves. We are presently attempting to get more stenotic porcine valves from both manufacturers.

We have postponed the start of the velocity measurement studies to November 1 due to the problems and questions we raised in our letter of October 19, to Dr. Letzing. Pulsatile flow velocity and pressure drop measurements are scheduled to start November 1.

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

Period: 11/1/81 - 11/30/81

During the month of November the steady flow pressure drop measurements were completed. Pulsatile flow pressure drop and regurgitation studies are presently in progress and we hope to finish them before the Christmas vacation. Pulsatile flow visualization studies are also presently in progress.

We have not started the velocity measurement work mainly due to equipment problems. We have just received (11/30) equipment to convert the LDA to a 3-beam system. The PDP 11/03 mini-computer, which is interfaced on-line to the LDA system, had hardware problems for about a week. We intend to start the LDA studies the week of 12/7/81. We are, however, still awaiting a reply to our letter of 10/19/81.

A detailed progress report for the period 10/1/81 through 12/31/81 will be provided next month.

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

Letter Report (1/1 - 1/31/82)

During the past month progress on the project was very slow due to two major reasons. A major snow storm in Atlanta closed Georgia Tech for a week. In addition, we had major problems with the new laser - Doppler equipment. The equipment was shipped to the manufacturer for repair and was returned to us on January 29. During the coming week we will put the LDA system back together again.

During January we finished the leaflet photography experiments. We have also been analyzing the steady and pulsatile flow pressure drop and regurgitation results collected last year. After a complete analysis of this data, any experiments that have to be repeated will be scheduled. The pulsatile flow visualization films were also processed during the past month.

Since no written changes have been made to the contract the velocity and shear stress measurements will proceed as according to the original contract and our original proposal. Unless the changes we have discussed with Dr. Letzing are made officially by February 28, 1982, it may not be possible to incorporate the modifications into the contract without cost overruns. Please note that we requested for a contract modification on October 19, 1981.

Dr. Letzing has requested that we study two Hall-Kaster valves in this contract. Money to purchase these valves, however, is not available in the budget. We discussed the possibilities of using two Hall-Kaster valves provided a couple of years ago by Medtronic Blood Systems, Inc. to Dr. Yoganathan. Since these valves were provided to an independent investigator, it is our current feeling that there may be legal ramifications if these valves were used in the FDA study. We therefore suggest that money be provided to purchase the two Hall-Kaster prostheses ($2500).

PROSTHETIC HEART VALVES: A STUDY OF

IN VITRO PERFORMANCE

Letter Report (2/1-2/28/82)

Over the past month the buffer unit on the LDA system malfunctioned once again. The unit was returned to the manufacturer for warranty repair. Therefore during the past month we have made some preliminary steady flow velocity measurements in the aortic flow section. Without the buffer unit shear stress measurements were not possible.

We are still analyzing the pressure drop, regurgitation, flow visualization, and leaflet photography data we collected over the past 3 to 4 months. Any experiments that have to be redone due to the analysis of this data, will be conducted during March and the first two weeks of April.

During the month of February we received written comments from Drs. W. Letzing and S. Hilbert of the Bureau of Medical Devices, FDA, on the draft Phase I report. Their comments and suggestions are presently being incorporated into the final Phase I report. This report is being put on the Georgia Tech Cyber computer system word processor.

APY:lw

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

Letter Report (4/1 - 4/30/82)

Over the past steady flow velocity measurements have been conducted in the aortic position. The following valves have been studied at a steady flow rate of 417 cm^3/s: (i) St. Jude Medical bi-leaflet, (ii) Starr-Edwards 1260 ball, (iii) Ionescu-Shiley pericardial, (iv) Bjork-Shiley tilting disc and (v) Hall-Kaster tilting disc. The results from these preliminary studies will be analyzed during the next month. If these results are satisfactory, pulsatile flow velocity measurements should start in June.

The reason for starting with the steady flow studies was to understand the proper operation of our new 3-beam (2-dimensional) LDA system. It would have been technically futile to try the system out for the first time on a pulsatile flow field. The consequences could have been disasterous.

We have completed our analysis of the pressure drop, flow visualization and leaflet photography data. Approximately a half dozen experiments have to be repeated to complete the data collection for this phase of the experimental study. These experiments will be completed this month.

The final version of the phase I report was completed and should have reached the FDA by now. It is our opinion that phase I was a great success.

Letter Report (6/1 - 6/30/82)

During the month of June we moved our experimental facilities to a larger laboratory area. The move was necessitated by the growth of our research group, its activities and associated research equipment. We also purchased a PDP 11/23 MINC mini-computer system (Digital Equipment Corp.) to be interfaced with the 3 beam (two dimensional) laser-Doppler anemometer system. We are currently working on modifying our old software for on-line data collection and analysis. We anticipate that the software modification should be completed by the end of July.

During mid-June we started the pulsatile flow velocity measurements in the aortic flow channel. We have so far conducted experiments on the St. Jude bi-leaflet and Bjork-Shiley tilting disc valves. We hope to complete the experiments in the aortic flow channel by the end of August, if no equipment problems arise. Measurements are being made downstream of the valves at mid-acceleration, peak systole and mid-deceleration. At each spatial location at a fixed instant in the cardiac cycle at least 1000 data points are being collected. The collected data is being checked for its accuracy and statistical validity. Due to vibrations of the pulse duplicator system we are currently having problems measuring the wall shear stress accurately. At present we are able to measure velocities within 0.2 mm from the flow channel wall. We are attempting some new experimental procedures which we hope would allow us to measure velocities closer to the wall.

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

Letter Report (7/1 - 7/31/82)

Professor Yoganathan was away in Europe during the month of July attending the 3rd International Conference on Mechanics in Medicine and Biology at Compeigne, France, and visiting Bio-Fluid Dynamic Laboratories in Western Europe. At the 3rd ICMMB he presented a paper on the work conducted under Phase I of this project. The paper was well received. During the trip, many questions were raised about the Bureau of Medical Devices' current testing guidelines and clinical trail procedures for new prosthetic heart valves. It appears that within the next year or two West Germany and Great Britain are going to have in-house in vitro testing procedures, that will probably be more extensive and sophisticated than the current draft BMD guidelines require.

While Dr. Yoganathan was away in Western Europe the pulsatile flow velocity measurements in the aortic positions were continued by his graduate students. However, in mid-July problems developed with the Georgia Tech campus air compressor. The compressor leaked an unusually large amount of oil into the air supply system, and this caused the three-way quick acting solenoid valves on the pulse duplicator system to malfunction. We, therefore, have had to order new solenoid valves, which should arrive by mid-August. Pulsatile flow velocity measurements have been conducted on the: St. Jude bi-leaflet, Bjork-Shiley, Hall-Kaster and Ionescu-Shiley heart valves. If the new solenoid valves arrive as promised (by the vendor) by 8/15/82, we still hope to finish the experiments in the aortic flow channel by the end of the month (see Letter Report: 6/1 - 6/30/82).

Prosthetic Heart Valves: A Study of In Vitro Performance

Letter Report (9/1 - 10/5/82)

During the past month we have been writing computer programs on the MINC 11/23 mini-computer system, to analyze the pulsatile flow velocity data collected in the aortic flow chamber. We hope to complete the analysis of this data sometime this month. It is planned to start the mitral chamber measurements by November 1. Due to the delays we have had and the large amounts of data collected, we have requested a three month no-cost extension to the project. This would terminate the project on 2/28/83. We feel this extension is necessary for us to complete the project in a satisfactory scientific manner.

We are still attempting to find a paint that will adhere on to the surface of the Starr-Edwards ball during pulsatile flow. I have discussed the problem with Dr. E. Mueller at the Center for Medical Device Analysis. He is also looking into the problem. The Ionescu-Shiley pericardial valve that was purchased for the project developed a cuspal tear (fatigue) during the aortic velocity measurements. This valve can no longer be used. The valve will be returned to Dr. Mueller. Therefore, it will not be possible to conduct further studies on the Ionescu valve.

Prosthetic Heart Valves: A Study of In Vitro Performance

Letter Report (10/1 - 10/31/82)

During the month of October we continued to analyze the pulsatile flow velocity data obtained in the aortic flow chamber. Most of the data appears to be in good order. It is, however, apparent that some of the experiments may have to be repeated to check for scientific accuracy and consistency.

The pulsatile flow velocity measurements in the mitral flow chamber will be started in November. The following valves are to be studied: (i) Beall disc valve, (ii) Hancock porcine valve, (iii) Bjork-Shiley (c-c) tilting disc valve, (iv) Hall-Kaster tilting disc valve and (v) St. Jude Medical bi-leaflet valve. Flow visualization studies conducted earlier in the project, indicate that the flow fields downstream of the Beall disc and Hancock porcine valves are relatively symmetric. Therefore with these two valve designs, it is proposed to make velocity measurements only across the central diameter of the prosthesis. With all five valves measurements will be made during: (i) mid acceleration, (ii) peak diastole and (iii) mid deceleration, downstream of the prostheses. In addition, measurements will be made upstream of the prostheses during valve closure.

We have had no luck finding a paint that will adhere to the surface of the Starr-Edwards (1260) ball valve. We may have to resort to taping the surface of the ball. Doing so may effect the hydrodynamic performance of the ball. We will have to wait and see till we attempt the experiment.

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

Letter Report (12/1/82 - 1/7/83)

During the month of December, pulsatile flow velocity measurements were conducted in the mitral flow chamber. Measurements were completed on the Beall, St. Jude, and Bjork-Shiley heart valve prostheses. Partial measurements have been made on the Hancock porcine valve. On 12/24/82 one of the frequency counters of the LDA system malfunctioned. The unit was shipped to manufacturer for repair and is expected back in our laboratory on 1/10/83. The LDA experiments will continue as soon as the frequency counter arrives.

On 1/7/83 Dr. Yoganathan met with Drs. W. Letzing and E. Mueller of the Bureau of Medical Devices, FDA to discuss the format for the final report on the project. Various options and formats were discussed, and will be outlined in a future memorandum to be written by Dr. Letzing. We anticipate starting work on a draft of the final report on 1/17/83.

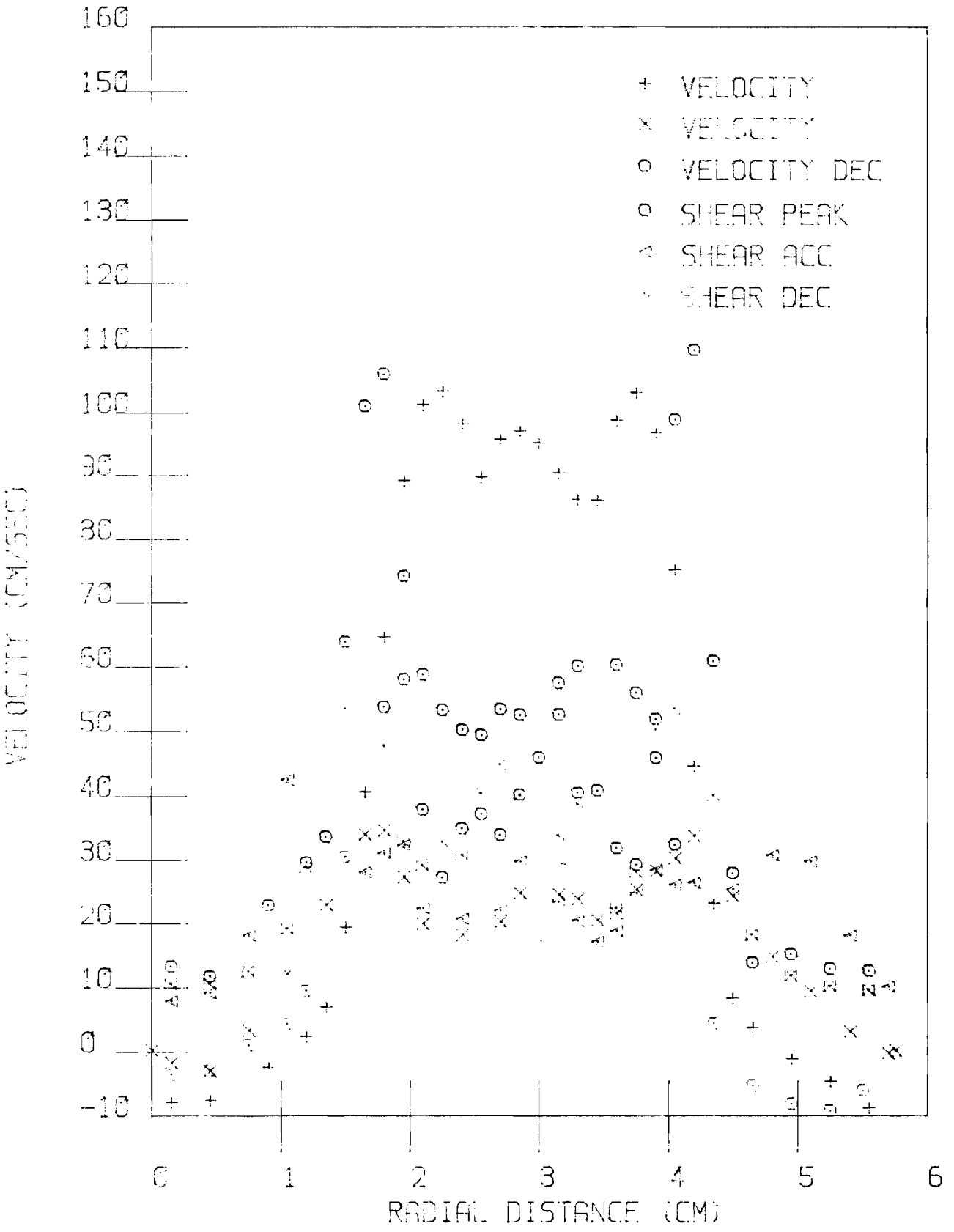
PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

Letter Report (1/8/83 - 2/3/83)

As reported in our last months report, one of the frequency counters had to be shipped back to the manufacturer (DISA Electronics) for repair. The counter was not returned to us until 1/17/83. Since then we have completed pulsatile velocity measurements on the Hancock porcine and Hall-Kaster tilting disc valves in the mitral position. We received a new Ionescu-Shiley valve from Shiley Laboratories on 1/28/83. Some pulsatile velocity measurements have been done on this valve.

We are just beginning to work on a draft of the final report. With that in mind three types of plots are enclosed. Figure 1 contains three velocity profiles and the corresponding three shear stress profiles in pulsatile flow. Figures 2 and 3 show the velocity and shear stress profiles separately. It is our opinion that Figure 1 is far too busy and that the pulsatile velocity and shear stress data should be presented independently as in Figures 2 and 3. It also appears that instead of using multiple colors, three symbols (in black ink) would be preferable. We would appreciate any comments from Dr. Letzing on this matter.

Fig. 1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VELOCITY (CM/SEC)
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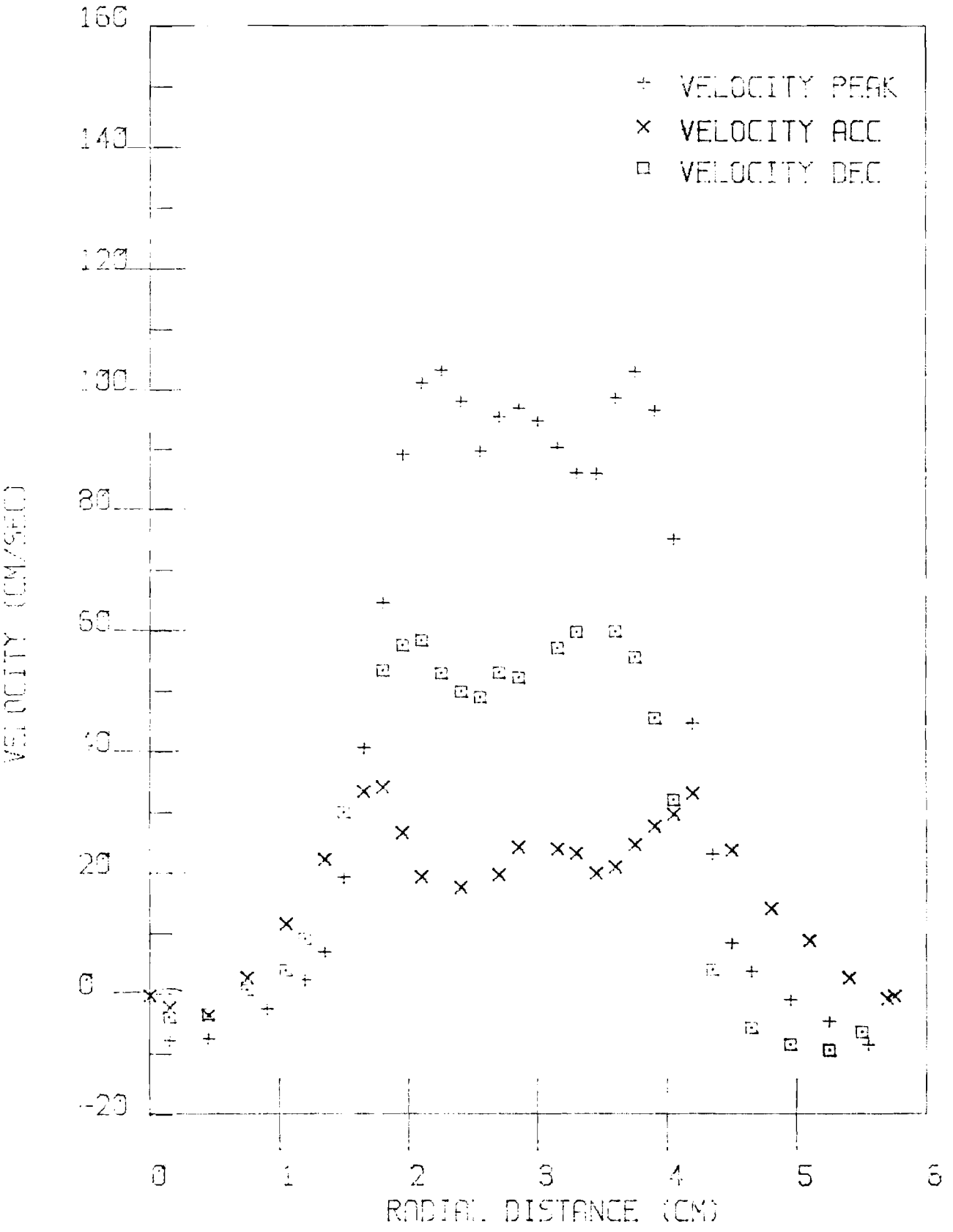
Fig 2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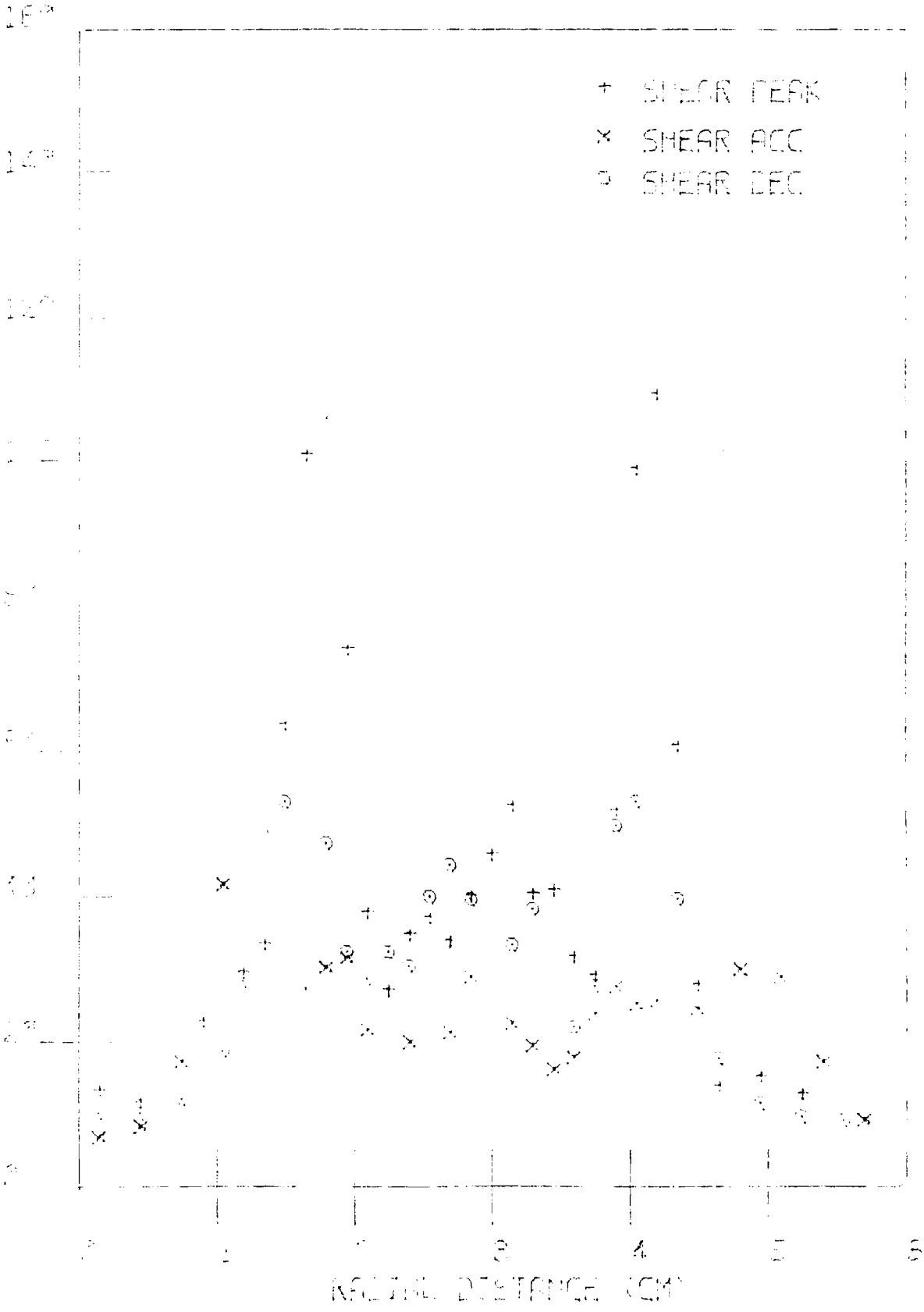
VELOCITY (CM/SEC)
RADIAL DISTANCE (CM)

Fig 3



PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE (January 18, 1982)

Progress Report: 10/1/81 - 12/31/81

During this period all steady flow pressure drops and flow visualization studies were conducted. The studies were conducted in appropriate aortic and mitral flow chambers over a steady flow rate range of 10 to 30 l/min (167 to 500 cm^3/s). We are presently analyzing the results of these steady flow studies. The initial results indicate that the prosthetic valves studied can be listed in the following order of increasing stenoticity: St. Jude, Hall-Kaster, Bjork-Shiley (C-C), Ionescu-Shiley, Hancock (MO), Smeloff, Carpentier-Edwards, Starr-Edwards, Hancock (std) and Beall. These results clearly indicate that the new low profile mechanical valves create smaller pressure drops compared to the older mechanical valve designs (caged-ball, caged-disc), and the porcine tissue valves with "average" muscle-shelf leaflets.

As an example of the results of the flow visualization studies are given below with appropriate photographs.

Bjork Shiley (Convexo Concave): Aortic Position, Steady Flow Visualization

The Bjork Shiley is a tilting disc valve. The circular occluder is free-floating and opens off-center. It is suspended between two eccentrically situated stelite struts. Since the disc does not pivot on the tube cross-section diameter, two asymmetric orifices are formed in the open position. In the photographs the valve is oriented such that the disc is seen from the side. It is not visible since it is black. Flow is from left to right. The larger, or major, orifice is above the disc. The jet through this orifice is seen above the shadow formed by the disc and slants upwards from left to right. The minor orifice jet appears to come out of the shadow in

the 25 l/m photograph. It is less visible in the 15 l/m photograph but is there.

15 l/m

At the low flow rate problems with low particle concentration were encountered,but essential details are visible. The major orifice jet slants upwards from left to right and impinges on the tube wall about 20 mm downstream of the valve. Flow separation is visible above the major orifice jet adjacent to the sewing ring. This causes a region of stagnation next to the sewing ring. Flow separation is also visible below the major orifice jet and above the minor orifice jet. The region of stagnation between these separations is directly downstream of the occluder. The minor orifice jet appears much broader than the major orifice jet and the flow is slower (shorter streaks). Although not visible in the photograph, observation revealed flow separation below the minor orifice jet adjacent to the sewing ring. This caused a region of stagnation next to the sewing ring. Farther downstream of the valve flow is very rapid downstream of the major orifice along the wall and much slower throughout the rest of the tube. This causes turbulence to persist downstream of the valve.

25 l/m

At the high flow rate the same flow details are there with some slight differences. The regions of stagnation appear smaller and are better defined by flow separation. Also, a greater turbulence intensity is visible downstream of the valve.

Consequences of observed flow patterns

Flow separation and regions of stagnation can lead to thrombus formation in the body. Clots on the downstream face of the disc have been observed

clinically (11,41). The low flow through the minor orifice combined with flow separation and stagnation adjacent to the sewing ring could lead to thrombus formation and excess tissue growth in this region. Excess tissue growth on the sewing ring around the minor orifice, sometimes leading to value dysfunction, has been observed clinically (11,41). The stagnation and flow separation above the major orifice jet would be less likely to cause thrombosis or excess tissue growth due to rapid swirling caused by proximity to the jet. The high turbulence caused by the major orifice jet could cause some blood cell damage leading to hemolysis and the release of clotting factors. The major orifice jet impinges on the wall about 20 mm downstream of the valve. Some damage to the endothelial tissue could occur. However, compared to a ball or flat disc valve, the chance of tissue damage would be less. This is because the angle of incidence is less than that of a ball or flat disc valve at a similar flow rate.

Smeloff Sutter: Mitral Position

Steady Flow Visualization

10 l/m

Flow is from left to right. The streamlines upstream of the valve appear to be parallel. Thus this valve does not appear to disturb the flow upstream of itself. The ball presents a large obstruction to flow causing significant radial flow. An angled jet can be seen which impinges on the wall at a location approximately even with the top of the cage. This jet could cause endothelial damage. This has been clinically observed in the aortic position (439). The turbulence caused by this jet, as well as the flow separation, could cause hemolysis and release of clotting factors. This has been observed clinically in some cases. Flow separation is seen

to the left of the jet causing a stagnation region adjacent to the sewing ring. In the body excess tissue growth and thrombus formation could occur here leading to possible valve dysfunction. The bases of the struts are in this flow separation/stagnation region and thrombus or excess tissue growth could occur there also. The separation caused by the struts themselves could also lead to similar problems. This separation was not visible here due to the orientation of the sheet of light above the valve and its width being comparable to that of the strut. Excess tissue growth on the sewing ring (262, 278) and thrombus formation on the downstream struts where they join the metal orifice ring (185, 263, 267, 268, 283, 284, 372, 439) have been observed clinically. Thrombus formation at the junction of the upstream struts and the metal orifice ring has also been observed clinically.

The jet separates from the ball about 1/2 way around it. This leaves a region of stagnation downstream of the ball. The ball is rapidly moving in the body so that thrombus formation on it is very unlikely. The ends of the struts extend into this stagnation zone. However they appear to be washed by the"swirling fluid"due to the proximity of the jet. The most stagnant zone appears to be directly downstream of the center of the ball. Since the struts do not extend into this region, thrombus formation would probably not occur. Indeed this has not been a problem clinically unlike the Starr Edwards valve whose struts meet at the cage apex.

The flow field downstram of the valve is very turbulent. Rapid flow along the walls eventually dissapates into large swirls resulting in some reverse flow along the center of the tube. This reverse flow tends to wash part of the ball and the downstream ends of the struts. It could also lead to ball instability. However, this was not observed for the Smeloff Sutter in the mitral position.

25 l/m

At the higher flow rate the jet is more nearly horizontal and separates from the ball approximately 3/4 of the way around. A triangular shaped stasis region is clearly seen. The strut ends extend into this region but are washed by swirling fluid at the edge of the stagnation zone. The stagnation region behind and beside the ball, adjacent to the sewing ring, is much larger. Thus the problems of thrombus formation and tissue overgrowth on the sewing ring and at the strut bases would be expected to be worse.

The flow pattern downstream of the ball is somewhat reversed compared to the low flow rate. The jet no longer impinges on the wall but travels down the center of the tube. This dissapates into swirls resulting in some reverse flow along the walls.

Hancock (Modified Orifice): Aortic Position (Symmetric Section)

Steady Flow Visualization

10 l/m

This tissue valve has a centrally opening orifice which causes a central jet. This jet is well defined in the photograph. It extends at least 40 mm downstream of the valve sewing ring before dissipating. Flow separation occurs at the edge of the leaflets causing a region of stagnation adjacent to the sewing ring and the out flow faces of the leaflets. It extends about 20 mm downstream of the valve. This would be a very probable site for thrombus and excess tissue growth formation. Both of these have been observed clinically (112, 194, 320, 324, 331, 332, 339, 350, 355, 356, 360, 315, 325, 327, 333, 341, 343, 381). It may also encourage califc deposits on the out flow faces of the leaflets.

The turbulence caused by this central jet is still visible 150 mm downstream of the valve when compared to the parallel streaks upstream of the valve. This could lead to some hemolysis which in fact has been observed clinically in the mitral and tricuspid positions.

25 l/m

At a higher flow rate the well defined jet extends to about 60 mm downstream of the valve. The stagnation region on the wall adjacent to the sewing ring extends about 40 mm downstream of the valve.

In addition, most of the pulsatile flow pressure drop, regurgitation and flow visualization studies have been conducted in both aortic and mitral flow chambers. The data from these studies are at present being analyzed in detail. Results from the pulsatile flow studies will be discussed in our next 3 month progress report.

We are presently conducting leaflet photography studies on the tissue bioprostheses. Thexe experiments should be completed by the end of January. We have received all the equipment from DISA Electronics to convert our LDA system to a 2-D velocity measurement system. This system will allow us to measure axial and radial velocities and turbulent shear stresses on-line. Unfortunately, some of the new equipment we received is not functioning properly. As indicated in our letter of December 8 , 1981 two pieces of equipment were returned to DISA. Further LDA equipment, problems developed immediately after the Christmas vacation. These problems got worse during the first week of January. Therefore, the pieces of equipment which were malfunctioning were shipped to DISA on January 12. All the equipment is under warranty, and it is our hope that it will be returned to us within the next ten days. As soon as the LDA 2-D system is fully operational, the detailed pulsatile flow velocity and shear stress measurements will begin.

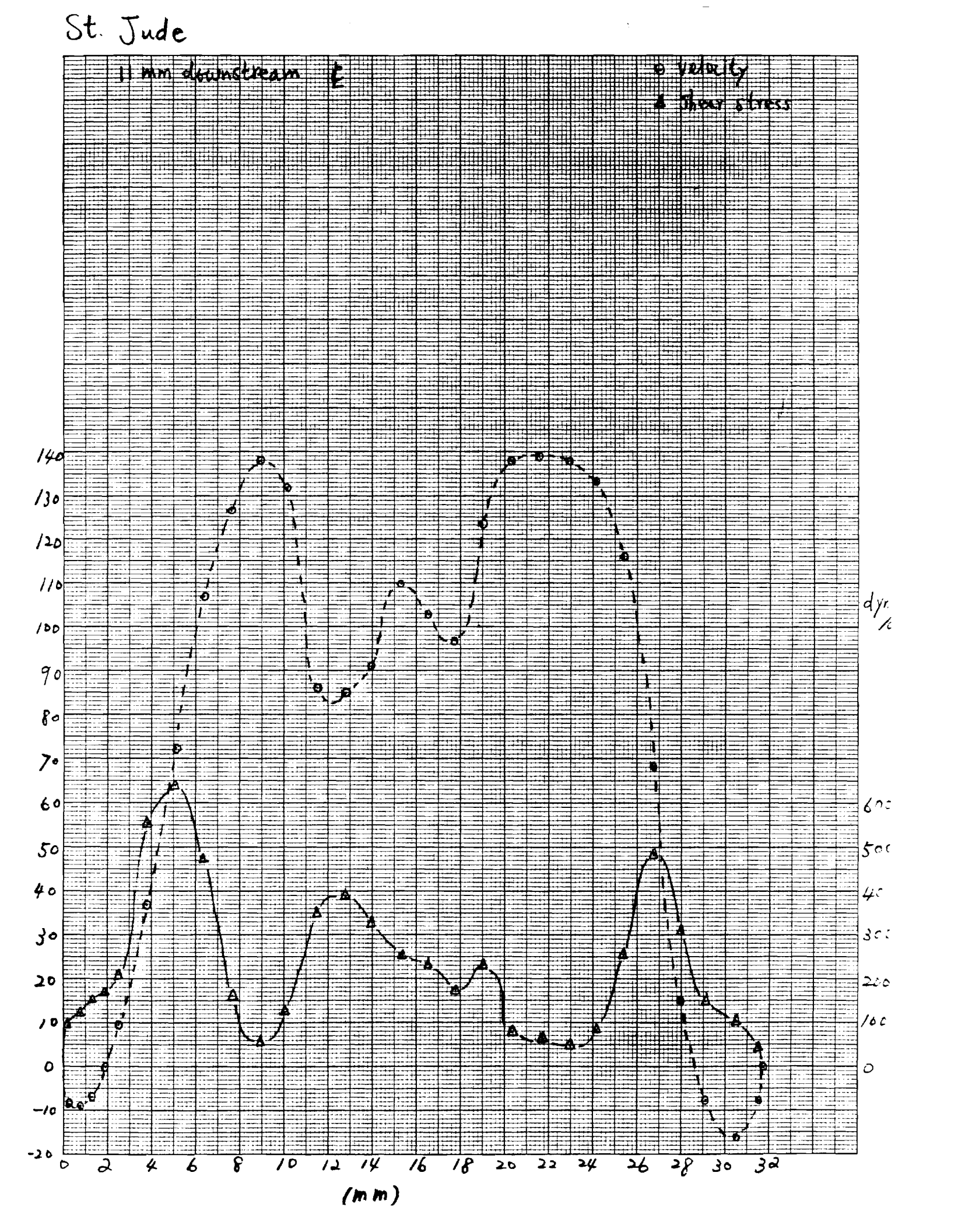
PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

Progress Report: 1/1/82 - 3/31/82

Progress during this three month period was extremely slow. The primary reason was the equipment failure problems we encountered with the laser-Doppler anemometer system. Most of these problems appear to have been corrected. Steady flow velocity and shear stress measurements were begun with the 3-beam LDA system in mid-March. By the second week of February we received comments on the draft Phase I report from Doctors Letzing and Hilbert of the Bureau of Medical Devices. Their comments have been incorporated into the final version of the report. The report is presently being typed on a word processor and should be completed by mid-April.

The steady pulsatile flow pressure drop, regurgitation, flow visualization and leaflet photography data were analyzed. Some of the pulsatile flow data is still being analyzed. Experiments that needed to be repeated were conducted during this period. One of the graduate students who worked on the project is planning to write his MS thesis this quarter. His thesis will contain most of the steady and pulsatile flow results (other than the pulsatile flow visualization, and all the velocity and shear stress measurements). Attached are some preliminary results of the steady flow velocity measurements.

It is our hope that during the next three months all the steady flow velocity measurements will be completed in the aortic flow section. We also plan to start the pulsatile flow velocity studies in the aortic position.


St. Jude
11 mm downstream
velocity
shear stress
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
(mm)
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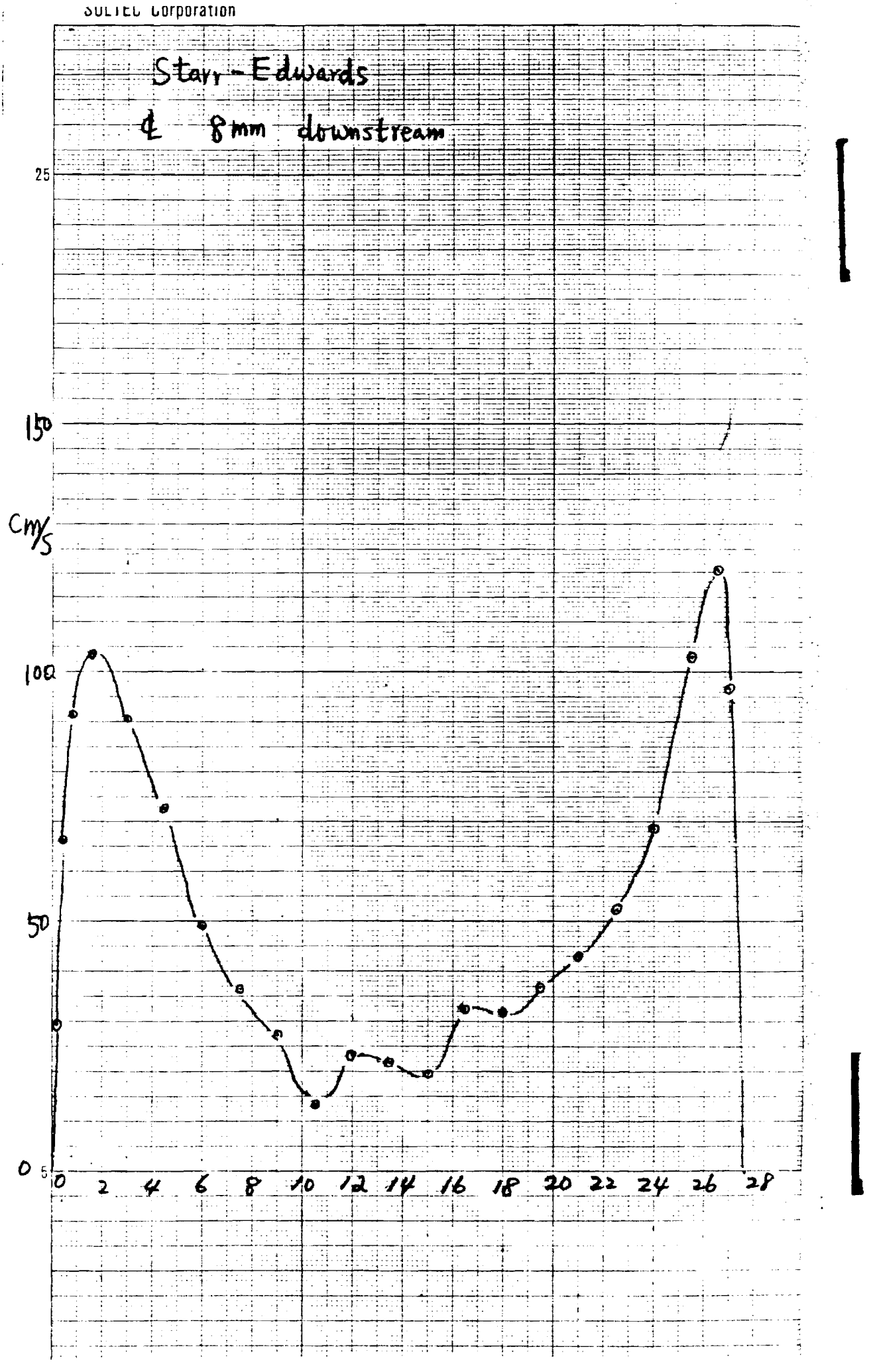
20
10
0


Starr-Edwards
℄ 8mm downstream
25
150
Cm/s
100
50
0
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

Progress Report: 1/1/82 - 5/31/82

Progress during the first three months (1/1 - 3/31/82) was extremely slow. The primary reason was the equipment failure problems we encountered with the laser-Doppler anemometer system (see attached letters). Most of these problems appear to have been corrected. Steady flow velocity and shear stress measurements were begun with the new 3-beam laser-Doppler anemometer system in mid-March. By the second week of February we received comments on the draft Phase I report from Drs. Letzing and Hilbert of the Bureau of Medical Devices. Their comments have been incorporated into the final version of the report. The final Phase I report was completed, typed on a word processor and mailed to BMD by May 10, 1982.

The following items have been completed in accordance with the contract and our research proposal.

1. Phase I with final report submitted on or around May 10, 1982

2. Steady flow pressure drop measurements on the Starr-Edwards (1260 and 6120), Smeloff, Bjork-Shiley, Hall-Kaster, Beall, St. Jude, Hancock (std. and mo), Carpentier-Edwards and Ionescu-Shiley valves in both aortic and mitral chambers. Experiments were conducted at various steady flow rates in the range of 5 to 30 ℓ/min.

3. Pulsatile flow pressure drop studies have also been conducted on the above valves in the aortic and mitral chambers, at a cardiac output range of 2-5 to 7-5 ℓ/min. In these experiments the mean systolic or diastolic pressure drops, and Q_{rms} flow rates were measured at four different cardiac outputs. The data was all collected from the Georgia Tech pulse duplicator system via the Apple II plus micro-

processor system. From these measurements the effective orifice areas and performance indicies of the different valve designs have been obtained.

4. Pulsatile regurgitation studies in both aortic and mitral chambers have been completed on all the valves except the Smeloff. According to the manufacturer of the Smeloff valve, this valve design has to be tested at $37^{o}C$ in order to measure its proper regurgitant characteristics. We are presently unable to do this on our pulse duplicator system. The pulse duplicator can only be operated at room temperature ($\sim 22^{o}C$).

5. Steady and pulsatile flow visualization studies have been conducted on all the above valves in both chambers at physiologic conditions. The photographs were taken in the immediate vicinity of the valve prostheses. We now have a library of negatives on the flow visualization characteristics of the different designs. From these photographs we have been able to make detailed qualitative as well as semi-quantitative observations. In doing these experiments we had to experiment with different types of particles, films (ASA, etc.), and camera settings.

6. Leaflet photography studies have been conducted on the Hancock (Std. and mo), Carpentier-Edwards and Ionescu-Shiley tissue valves, at two cardiac outputs. We are still in the process of measuring the leaflet opening areas from the photographs (slides).

7. Over the past two months steady flow velocity and shear stress measurements have been conducted in the aortic position. The following valves have been studied at a steady flow rate of 417 cm^3/s: (i) St. Jude Medical bi-leaflet, (ii) Starr-Edwards 1260 ball, (iii) Ionescu-Shiley peri-

cardia, (iv) Bjork-Shiley tilting disc and (v) Hall-Kaster tilting disc. Velocity measurements (axial and radial) were made along the flow channel centerline at at least two downstream locations. For the asymmetric flow fields, measurements were made off-centerline as well. Across each diametric traverse, measurements were made at 10 - 15 points. At each point 1000 - 2000 data samples were collected. These sample sizes give statistically valid data. The results from these preliminary studies are still being analyzed. If these results are satisfactory, pulsatile flow velocity measurements should start in June. The reason for starting with the steady flow studies was to understand the proper operation of our new 3-beam (2-dimensional) LDA system. It would have been technically futile to try the system out for the first time on a pulsatile flow field. The consequences could have been disasterous.

The following work has yet to be completed:

1. Pulsatile flow velocity and shear stress measurements in the aortic flow chamber for the Starr-Edwards, Bjork-Shiley, St. Jude, Hall-Kaster, Porcine and Ionescu-Shiley valves.

2. Pulsatile flow velocity measurements in the mitral chamber for the Beall, Bjork-Shiley, Hall-Kaster, St. Jude and Porcine (probably Hancock std.) valves.

It is planned to start the pulsatile flow aortic studies in June. Barring any unforseen problems we hope to complete the entire study within the next six months. We have therefore, requested a 3-month no-cost extension to the project. The pulsatile velocity and shear stress measurements will be performed under the appropriate physiologic conditions, as well as data collection procedures, such that the final data that will be presented to the FDA

is statistically valid and is of good quality. If any technical problems arise during the next six months, we will inform Dr. Letzing of such problems in our monthly reports.

PROSTHETIC HEART VALVES: AN IN VITRO STUDY

Progress Report: 6/1/82 - 9/6/82

During the month of June we moved our experimental facilities to a larger laboratory area. The move was necessitated by the growth of our research group, its activities and associated research equipment. We also purchased a PDP 11/23 MINC mini-computer system (Digital Equipment Corp.) to be interfaced with the 3 beam (two dimensional) laser-Doppler anemometer system. We had to modify our old software for on-line data collection. We are currently modifying the data analysis software so that it is compatible with the PDP 11/23 system.

Professor Yoganathan was away in Europe during the month of July attending the 3rd International Conference on Mechanics in Medicine and Biology at Compeigne, France, and visiting Bio-Fluid Dynamic Laboratories in Western Europe. At the 3rd ICMMB he presented a paper on the work conducted under Phase I of this project. The paper was well received. During the trip, many questions were raised about the Bureau of Medical Devices' current testing guidelines and clinical trail procedures for new prosthetic heart valves. It appears that within the next year or two West Germany and Great Britain are going to have in-house in vitro testing procedures, that will probably be more extensive and sophisticated than the current draft BMD guidelines require.

Steady flow velocity and shear stress measurements were made in the symmetric aortic flow channel at a flow rate of 417 cm^3/s (25 ℓ/min). This steady flow rate corresponds to the peak systolic flow rate at a cardiac output of about 4 to 5 ℓ/min. All measurements were made within a downstream distance of 30 mm from the valve sewing ring. The closest possible downstream measurement location varied depending on the valve design. The valve designs studied were: Bjork-Shiley and Hall-Kaster tilting disc valves; St. Jude bi-leaflet valve; Starr-Edwards (1260) ball valve; and Ionescu-Shiley pericardial

tissue valve. Most of the measurements were made in the forward scatter mode. The back-scatter mode was, however, employed to obtain measurements in the annular flow region created by the ball and tissue valves. With the 3 beam LDA system both axial and radial velocities were measured simultaneously. Each full profile consisted of about 15 - 20 data points. For each data point at least 1024 samples were collected and analyzed, to calculate mean velocity, normal stress, shear stress and rms turbulence quantities. With the tilting disc valves velocity measurements were made in the major orifice, minor orifice and along the center line. With other valve designs, measurements were made along the center line and above the center line. No measurements were made below the center line since flow visualization studies indicated that the flow fields were relatively symmetric about the center line.

Pulsatile flow velocity measurements were made in the immediate vicinity of the Bjork-Shiley, Hall-Kaster, St. Jude, Starr-Edwards (1260) and Ionescu-Shiley heart valve prostheses. Experiments were conducted at a heart rate of 70 beats/min, systolic time of about 300 ms, physiological pressures and cardiac outputs of about 5 to 6 hours ℓ/min. Measurements were made at the same locations the steady flow studies were conducted. A 20 to 30 ms time step was used for data collection. Data was collected at three different time instances during systole, namely: (i) mid-acceleration, (ii) peak systole, and (iii) mid-deceleration. As in the steady flow experiments, a full profile consisted of about 15 - 20 data points. For each data point at least 1024 samples were collected. In addition to the downstream measurements, measurements were also made upstream of the valves to study the regurgitation patterns of the different valve designs. Measurements were taken at the time of highest closure backflow and at mid-diastole. In pulsatile flow wall shear stress measurements were also conducted. Since only the axial velocity component is needed to calculate the wall shear stress, a two beam LDA set up was employed to increase the accuracy of the measurements. The closest data points were between 0.03

to 0.06 mm from the flow channel wall.

When conducting measurements with the Starr-Edwards ball valve in the back-scatter mode, it was necessary to paint the poppet black to reduce the interference from the reflected light. However, none of the black points we tried remained attached to the poppet surface in pulsatile flow. The paint peeled-off within a couple of minutes. Therefore, we have not conducted any back-scatter measurements in pulsatile flow. We are, however, working on the problem.

Work to be done:

1. Analysis of the steady and pulsatile flow data obtained in the aortic flow channel.

2. Back-scatter measurements with the Starr-Edwards (1260) and Ionescu-Shiley valves in the aortic position.

3. Pulsatile flow velocity measurements in the mitral chamber for the Beall, Bjork-Shiley, Hall-Kaster, St. Jude and Porcine valves.

4. Analysis of data from item #3.

5. Write final report.

PROSTHETIC HEART VALVES: An IN VITRO STUDY

Progress Report: 9/7/82 - 12/1/82

Pulsatile flow forward-scatter velocity measurements were carried out to completion with the following aortic valves in the symmetric aortic flow channel: (i) Starr-Edwards (1260), (ii) Bjork-Shiley (C-C), (iii) Hall-Kaster, (iv) St. Jude, and (v) Ionescu-Shiley. Steady flow velocity measurements on these valves in the aortic flow channel were conducted previously. The pulsatile flow velocity measurements conducted in the aortic flow chamber are shown in Table 1. In addition, the studies that need to be completed in the aortic flow chamber are also indicated.

During the latter part of September and most of October, we were modifying the existing data analysis software and writing new data analysis software to be compatible with our new PDP 11/23 MINC system. The latter part of October was spent analyzing some of the data collected in the aortic flow channel. Balance of the aortic flow chamber data has yet to be analyzed.

We started the pulsatile flow velocity measurements in the mitral chamber during the first week of November. The data we, however, collected during the first week turned out to be useless due to poor signal-to-noise conditions. We also experienced problems with the pulse duplicator system in attempting to reproduce a satisfactory mitral flow curve. We therefore only started useful data collection in the mitral chamber on 11/15/82.*

In all pulsatile flow velocity experiments a 20 to 30 ms time step was used for data collection. Data was collected at three different times during systole/diastole (aortic/mitral): (i) mid-acceleration,

*Note: Georgia Tech was physically closed from 11/25 to 11/29 for Thanksgiving. It was not possible to conduct experiments during this period.

(ii) peak systole/peak diastole (aortic/mitral), and (iii) mid-deceleration. A full profile consists of 15 - 20 data points. For each data point at least 1024 samples were collected.

Work to be Completed:

Tables 1 and 2 indicate clearly the experiments that need to be completed, together with the estimated time for completion (in actual working days). It should be noted that the time estimates do not take into account any time that may be lost due to any equipment failures. In addition, the laboratory facilities at Georgia Tech will be physically closed from 12/23/82 to 1/3/83 for the Christmas period. After completion of the pulsatile flow velocity experiments, it is estimated that the data analysis will take about 30 - 40 days.

During this contract a vast amount of data has been generated. It is therefore estimated that the draft final report will take about 45 days to write. It is currently planned to start writing this report on 1/17/83. However, before we can start writing the report we need definite concrete input from the Dr. W. Letzing (project technical monitor), on or before 1/14/83. Any delays in this technical consultation will lead to delays in writing the final report. We need guidance from Dr. Letzing as to what should be in the final report, how it should be organized and structured, what material should be emphasized, etc. Most of the consultation could be conducted over the telephone and then finalized in writing.

TABLE 1: PULSATILE FLOW VELOCITY MEASUREMENTS

IN THE AORTIC FLOW CHAMBER

Name of Valve	Centerline Full Profiles Number	Centerline Half Profiles Number	Major Orifice Profiles Number	Minor Orifice Profiles Number	90° Profiles Number	Upstream Profiles Number	Estimated Time Needed to Complete Remaining Experiments Days
S - E (1260)	3✓	3+ 3✓	6**✓	--	--	2✓	2.5
SJM	3✓	3✓	6**✓	--	3✓	2✓	0.5
B-S	3✓	3✓	6**✓	6**✓	3✓	2✓	0.5
H-K	0*	3✓ 3	6**✓	6**✓	3	2✓	2.0
I-S	3✓	3✓ 3+	3**✓	--	--	1✓	2.5
Hancock (MO)	3	3+	--	--	--	1	4.0
C-E	3	3+	--	--	--	1	4.0
Wall Shear Stress							2.0
						TOTAL	18

✓ Indicates experiments completed

* Due to the larger opening angle of the H-K valve, in order to get a full profile with the 3 beam LDA we would have to make measurements about 40 mm downstream of the valve.

\+ Back-scatter measurements, if possible, in annular flow region between poppet/leaflet and flow channel wall

** Some of these are half profiles

TABLE 2: PULSATILE FLOW VELOCITY MEASUREMENTS

IN THE MITRAL FLOW CHAMBER

Name of Valve	Centerline Full Profiles Number	Centerline Half Profiles Number	Major Orifice Profiles Number	Minor Orifice Profiles Number	90° Profiles Number	Upstream Profiles Number	Estimated Time Needed to Complete Remaining Experiments Days
Beall	3✓	3✓	3**✓	--	--	1✓	0.5
SJM	3	3	6**	--	3	2	8.0
B-S	3	3	6**	6**	3	2	10.0
H-K	3*	3	6**	6**	3	2	10.0
Hancock	3	3+	3**	--	--	1	4.0
I-S	3	3+	--	--	--	1	4.0
Wall Shear Stress							3.5
						TOTAL	40

✓Indicates experiments completed

* If obstruction is not caused by the larger opening angle; otherwise 3 additional half profiles will be made

** Some of these are half profiles

+ Back-scatter measurements, if possible, in annular flow region between leaflet and flow channel wall

E-14-654

FINAL REPORT
Phase I

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

By

A. P. Yoganathan, Ph.D., Principal Investigator

Under

Contract No. 223–81–500

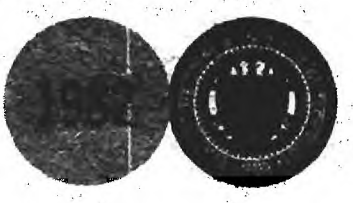
Georgia Tech Research Institute (GTRI)
and
Bureau of Medical Devices (BMD)
Food and Drug Administration (FDA)

Wm. Letzing, Ph.D., FDA Project Officer

Duration of Study: 7/1/81–9/30/81

April 1982

GEORGIA INSTITUTE OF TECHNOLOGY
A UNIT OF THE UNIVERSITY SYSTEM OF GEORGIA
SCHOOL OF CHEMICAL ENGINEERING
ATLANTA, GEORGIA 30332



PHASE I FINAL REPORT

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

April 15, 1982

Contract No. 223-81-500

between

Georgia Tech Research Institute (GTRI)

and

Bureau of Medical Devices (BMD),

Food and Drug Administration (FDA)

Principal Investigator: A. P. Yoganathan, Ph.D.

FDA Project Officer: Wm. Letzing, Ph.D.

Duration of Study: 7/1/81-9/30/81

ABSTRACT

In order to identify and define the fluid dynamic characteristics of primary importance in quantifying heart valve performance, GTRI has carried out a paper study of this subject under contract with the FDA. Where possible these fluid dynamic characteristics have been related to valve hemodynamics and clinical complications such as hemolysis, thromembolism, thrombus formation, tissue overgrowth and other valve dysfunctions.

This Phase I study is intended to provide a better understanding for the need to establish in vitro flow testing guidelines which encompass state-of-the-art instrumentation and methodology. The study indicates very clearly that there is more to the in vitro and in vivo fluid dynamic performance of a heart valve prosthesis other than pressure drop and regurgitation. The study also indicates the need for good clinical follow up data on heart valve recipients, analysis of sub-lethal and/or lethal damage to blood components and endothelial tissue, and detailed pathologic studies on recovered (at surgery and/or autopsy) valve prostheses.

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I. BACKGROUND AND INTRODUCTION

The major objective of this report is to attempt to correlate the in vitro fluid dynamic performance of prosthetic heart valves with their in vivo clinical and pathological findings. The aim is to clearly document any relationship between in vitro fluid dynamic performance and potential clinical and/or pathological findings and complications. In order to prepare this report and extensive study of appropriate and useful scientific literature (medical, and bio-medical engineering) was conducted.

Over 450 articles and books have been read and analyzed during a two month period (7/1/81-9/2/81). A majority of these articles and books have been published in the domestic literature during the past ten years. Important articles in the scientific literature were identified from a computerized literature search (MEDLAR) which was conducted at the start of the project. In addition, pertinent information was obtained from some of the valve manufacturers and by private communication with certain investigators. Articles were numerically cataloged as they were received and read. Therefore, the main text will not contain references in numerical order. In order to recatagorize the more than 450 articles would have taken too much valuable time. It should be noted that a draft report had to be completed in 3 months (7/1/81-9/30/81). Of these 3 months, 2 months were spent collecting and reading the articles. The third month was spent analyzing the material read, and writing the draft report. After consultations with BMD personnel on the draft report, a final report was prepared during March and April, 1982.

failure due to material fatigue or chemical change, (g) damage to the endothelial tissue lining of the vessel wall adjacent to the valve and (h) leaks caused by failure of the valve to close properly. Problems (a), (b), (e) and (g) are directly related to the fluid dynamics associated with the various prosthetic heart valves, and need to be addressed in more detail by investigators studying bio-fluid mechanics. The other problems are indirectly related to the fluid mechanics. The problems relating valve failure due to material fatigue or chemical change also need to be studied especially as they relate to bioprostheses.

Tissue bioprostheses gained wide spread use during the mid-1970's. It was even naively thought by some of the tissue valve manufacturers that the ideal heart valve prosthesis had been discovered. The major advantage of tissue bioprostheses compared to their mechanical counterparts is that they have a lower incidence of thromboembolic complications. Therefore, tissue valves for a large part can be used without anticoagulation therapy to eliminate or reduce thromboembolic complications. Unfortunately, the tissue bioprostheses clinically used at present also have major disadvantages such as: (a) relatively large pressure drops compared to some of the mechanical valves, especially in the smaller sizes, (b) jet-like flow through the valve leaflets, (c) material fatigue and/or wear of valve leaflets especially in children. Because of these and other drawbacks valve manufacturers are now developing new designs of mechanical valves such as the St. Jude, Hall-Kaster and Omni-Science prostheses, newer designs of bioprostheses and trileaflet valves made from polymeric materials.

directly related to the fluid dynamics associated with the various types of valve prostheses. Blackshear and his co-workers (430,431) suggest that the shear stresses required in the bulk of the flow to hemolyze red blood cells are about 40,000 dynes/cm^2. Nevaril and his co-workers (432) contend, however, that this value could be as low as 1500 dynes/cm^2. In vitro experiments (433-435) have also recently shown that platelets could be damaged by shear stresses of the order of 100-500 dynes/cm^2. A formed element such as a red blood cell which adheres to the vessel wall or to a foreign surface (such as the valve superstructure) may be damaged by shear stresses of the order of 10-10^2 dynes/cm^2 (430,431,436). Lloyd, et al., (408) indicate that sublethal damage to red blood cells could occur at shear stresses on the order of 500 dynes/cm^2 or less. A very recent study by McIntyre (441) indicates that the red blood cells of heart valve patients are more filterable in micropores than compared to normal subjects, due to sublethal damage to the red cells of valve recipients. Lethal damage to red blood cells causes hemolysis which in turn leads to anemia. Sublethal and/or lethal damage to red blood cells could also lead to platelet adhesion, aggregation and coagulation, resulting in thrombus formation. Mechanical damage to platelets (lethal and sublethal) will eventually lead to thromboembolic complications.

Fry (437,438) has conducted two studies on the effects of wall shear on the endothelial lining of the aortic wall. He found that the endothelial cells on the vessel wall could be damaged at wall-shear stresses of about 400 dynes/cm and could be eroded off the vessel wall at shear stresses of about 950 dynes/cm^2. He observed that when the

blood cells could adhere onto the vessel wall. If the adhered red blood cell is exposed is exposed to shears on the order of 10 to 100 dynes/cm^2 it will probably be lethally damaged and hemolyzed. Red blood cells contain ADP and a clot-promoting factor known as erythrocin. These substances are released into the plasma as a result of rbc hemolysis initiating both platelet aggregation and coagulation, which in turn may lead to thrombus formation.

The mechanical damage to the blood elements, as well as to the endothelial tissue of the adjacent vessel wall, may in addition trigger the complex biochemical reactions which could lead to the excess fibrous tissue overgrowth observed on some recovered heart valves. Therefore, large wall and bulk turbulent shear stresses could cause serious problems and complications *in vivo.*

It is also well known that regions of flow stagnation, flow separation and excessively low shear in immediate vicinity of the valve superstructure have been related to thrombus formation and/or excess tissue overgrowth on the prosthesis. The flow velocity, shear stress and pressure fields in the immediate vicinity of a given heart valve prosthesis design are directly related to the fluid dynamic characteristics of the prosthesis. Therefore, detailed *in vitro* fluid dynamic studies should help predict potential problems and complications that arise *in vivo* with different designs of prosthetic heart valves.

clinical problems related to the prostheses. The results should therefore reflect the in vivo hemodynamic performance of normally functioning prostheses. All the information presented in these tables were obtained directly from their respective articles. Valve areas (VA), or otherwise known as the effective orifice areas, were calculated by the various investigators from the Gorlin (405) or modified Gorlin (406) formulae. We will not discuss the pit-falls of these formulae since they are used in all cardiac catheterization laboratories. The in vivo valve areas give a good qualitative and/or quantitative ranking for the in vivo pressure drop characteristics of the various valves. If different valve designs were studied by the same investigators and/or at the same medical center, these results will have more quantitative significance. Even though the absolute values of VA may vary from center to center for a given valve design, the ranking of different valve types according to in vivo valve areas should generally be consistent. The main reasons for the variations in the absolute values from center to center are: (I) Inaccurate in obtaining cardiac catheterization data (pressures and flows), (ii) obtaining a statistically large enough patient population and (iii) different formulae used to estimate VA. The in vivo tables do not contain regurgitation data because this parameter cannot be quantitatively measured during catheterization, or other in vivo procedures.

In vitro pressure drop, flow rate, and regurgitation data were in most cases obtained directly from their respective articles. From these data the valve areas (VA) (ie: effective orifice area) were calculated from the following formula:

absolute values among the different investigators is because different types of pulse duplicators and flow chamber geometries have been used. It should, however, be noted that there is better quantitative agreement in the in vitro pressure drop and regurgitation data between different investigators, than with the in vivo hemodynamic data from different medical centers.

Information obtained from the in vitro flow visualization, and velocity and shear stress measurement studies will be discussed in the text.

All the hemolysis and thromboembolic complication tables were constructed from information extracted from their respective articles. As can be seen from these tables there is no consistent scientific manner in which data on hemolysis and TEC's are reported in the medical literature. Elevated LDH levels, and reduced and/or absent haptaglobin levels are good indicators of intravascular hemolysis. Reduced half-lifes of red cells and platelets are in our opinion one of the best ways of monitoring mechanical (shear) damage to blood elements. Such tests are infrequently done in a clinical environment. Early TEC's and deaths are defined as those occurring during the first 30 days after valve replacement surgery. TEC events are expressed where possible as patient ratios and/or as a rate (% per pt. yr.).

Based on these tables and other pertinent information in the literature, we have been able to draw certain conclusions about the hemolytic and thromboembolic potential of the different valve designs. The locations of thrombus formation, excess tissue growth and related valve dysfunctions will be discussed in the text.

Sizes and Dimensions

Size	Sewing Ring Diameter(mm)	Orifice Diameter(mm)	Primary Orifice Area(cm^2)
21A	21	13	1.41
23A	23	15	1.67
24A	24	15	1.79
26A	26	16	1.94
27A	27	17	2.16
29A	29	18	2.57
31A	31	19	2.89
20M	20	13	1.27
22M	22	14	1.54
26M	26	17	2.14
28M	28	18	2.49
30M	30	19	2.86
32M	32	20	3.24
34M	34	22	3.66

*Dow Corning Trademark
**Cabot Corporation Trademark
***DuPont Trademark

Sizes and Dimensions

Size	Sewing Ring Diameter(mm)	Orifice Diameter (mm)	Primary Orifice Area (cm^2)
19A	19+	12+	1.21
21A	21+	14-	1.43
22A	22+	15-	1.70
24A	24+	16-	1.89
26A	26-	17-	2.16
27A	27+	17+	2.36
29A	29+	18+	2.66
31A	31-	19+	2.92
23M	23-	15-	1.70
26M	26-	17-	2.16
28M	28+	18-	2.50
30M	30+	19+	2.92
32M	32+	21-	3.30

(iii) (Models 2400 Aortic and 6400 Mitral)

Models 2400 (aortic) and 6400 (mitral) Starr-Edwards composite track valve prostheses are closed single-cage hollow metallic ball valve prostheses. The cage struts, poppets, and metallic closure supports on the inner aspect of the base ring are made of Haynes Alloy No. 21* (Stellite Alloy No. 21) and are easily seen radiographically. The inner aspect of the cage struts has no cloth covering and hence no metal cloth contact. The rest of the cage struts are covered by tubular-knitted porous polypropylene cloth. The orifice cloth is made from siliconized multi-filament Dacron** thread which together with the exposed metallic supports produces a composite seating surface which the ball impacts at closure. The sewing ring is made of Teflon*** and polypropylene cloth over a silicone foam padding. The Model 2400 valve has 3-strut cage while the Model 6400 cage has 4 struts.

(b) In Vivo Results

The clinical hemodynamic results for the various designs of the Starr-Edwards ball valves are given in Tables 1-8. For the aortic prostheses, valve areas (VA's) of 0.92 to 1.9 cm^2 were calculated for valve sizes of 21 to 29 mm. For the mitral prostheses in the size range of 26 to 34 mm, VA's were in the range of 1.4 to 2.7 cm^2. These values are similar to those observed with other ball valve prostheses.

As Tables 11 and 12 indicate there are numerous articles on the hemolysis and thromboembolic complications created by the different designs of Starr-Edwards ball valves. The results in Table 11 indicate without a doubt that the completely cloth covered strut models 2300, 2310, 2320, 6300, 6310 and 6320 caused moderate and in many cases severe hemolysis (36,104,120,154,163,222). The models 2400 and 6400 tend to cause less hemolysis compared to the other cloth covered Starr-Edwards ball valves (56,97,104,295). The models 1200/1260 and 6120 non-cloth covered valves cause mild to moderate hemolysis. The thromboembolic complications (Table 12) seem to be greater with the non-cloth covered models (1200, 1260, 6000, 6120) compared to the cloth covered models (2300, 2310, 2320, 2400, 6300, 6310, 6320, 6400). This fact is substantiated in clinical studies conducted on both cloth and non-cloth covered models by the same group of researchers (60, 79, 195, 99, 104, 250, 424). According to Lefrak and Starr, the cloth covered valves have an embolus free rate of 95% at 3 years versus 81% for the non-cloth covered prostheses (412 p. 67). The TEC rates for the Starr-Edwards ball valves seem to be in the range 3 to 6.5% per pt. yr. with anticoagulation therapy and as high as 10% per pt. yr. without

TABLE 1

IN VIVO PRESSURE DROPS: STARR-EDWARDS 1200/1260 AORTIC VALVES

Tissue Annulus Size mm	Rest					Exercise					ref#
	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA$_2$ cm^2	
21	5		29 (13-54)		1.0 (0.7-14)						77
23	7		18 (1-32)		1.1 (0.8-1.5)						77
24	7		13 (6-26)		1.3 (0.9-1.7)						77
26	6		21 (16-26)		1.3 (1.1-1.5)						77
27	1		13		1.8						77

Table 3

IN VIVO PRESSURE DROPS: STARR-EDWARDS 2310 AORTIC VALVE

Tissue Annulus Size mm	Rest N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	Exercise N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	ref#
21	10	NA	18 (~10-60)	NA	1.16 (0.8-1.4)						26
23	12	NA	25 (~5-55)	NA	1.30 (0.8-1.8)						26
	8	15.4 (9-28)	NA	3.3 (2.8-4.3)	1.52 (1.20-1.64)						37
	5	18 (11-28) 6 mo	NA	3.5 (2.8-4.3)	1.51 (1.20-1.64)						27
		15 (11-31) 27 mo	NA	3.3 (2.4-3.7)	1.40 (1.23-1.60)						27
24	18	NA	11 (0-35)	NA	1.23						26
	3	12.3 (7-17)	NA	2.9 (2.6-3.1)	1.45 (1.38-1.52)						37
	3	12 (7-17)	NA	2.9 (2.6-3.1)	1.45 (1.38-1.52)						27
	5	10 (7-14)	NA	2.9 (2.7-3.1)	1.60 (1.31-1.70)						27

TABLE 4

IN VIVO PRESSURE DROPS: STARR-EDWARDS 2400 AORTIC VALVE

Tissue Annulus Size mm	Rest					Exercise					ref#
	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA$_2$ cm^2	
23	8	18.4 (7-46)	21.4 (2-54)	3.1 (2.3-3.7)	1.6 (0.9-2.3)						31
24	8	15.6 (5.3-29.8)	15.4 (1-34)	3.4 (2.6-4.1)	1.9 (1.5-2.8)						31

TABLE 6

IN VIVO PRESSURE DROPS: STARR-EDWARDS 6300/6300C MITRAL VALVES

Tissue Annulus Size mm	6300	Rest				Exercise				ref#
	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA$_2$ cm^2	
28	10	9.1 (5.6-12.5)		2.6 (1.9-2.4)	1.45 (1.25-1.85)						29
	25	7.3 (~1-16)		NA	1.65 (~1-2.8)						26
	9	8 (~5-13)		NA	1.78 (~1.2-2.2)						33
30	2	11.0 (10.7-11.3)		3.2 (2.4-3.9)	2.15 (2.11-2.19)						29
	15	7.1 (~2-16)		NA	2.06 (~1.0-2.5)						26
	6	8.9 (~5-17)		NA	1.85 (~1.5-2.3)						33
28 & 30	2M=6 3M=4	11.6±3.5** (8-17)		3.16±.84** (1.8-4.3)	1.65±.3** (1.2-2.1)		24.5±7.1** (14-37)		4.78±1.37** (3.0-7.0)	1.78±0.4** (1.3-2.7)	75
	6300C										
28	12	8.9 (3-21)		2.52 (1.8-4.0)	1.66 (1.2-2.2)		13.1 (~10-20)		3.02 (~2-4.2)	1.62 (~1-2.5)	28
30	5	5.7 (~4-8)		2.73 (~2.5-3.0)	2.11 (~1.5-2.5)						28

** ± SD

TABLE 8

IN VIVO PRESSURE DROPS: STARR-EDWARDS 6400 MITRAL VALVE

Tissue Annulus Size mm	Rest					Exercise					ref#
	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	
28	4	4.4 (2.8-7.0)		3.4 (2.5-4.9)	2.0 (1.4-2.7)						31
30	11	4.2 (1.3-6.3)		2.7 (2.0-4.3)	2.2 (1.5-3.1)						31
32	4	8.5 (3.7-14.4)		2.8 (2.2-3.3)	1.7 (0.7-2.3)						31

TABLE 9

IN VITRO PRESSURE DROPS: STARR-EDWARDS AORTIC VALVE

Tissue Annulus Diameter mm	Model #	$\bar{\Delta p}$ mmHg	CO ℓ/min	Q_{rms} ℓ/min	VA cm^2	RV cm^3/stroke	Ref #
19	1260		5.0		1.04		419 p. 181
21	1200	26.6	6.0			2.4(@75 min^{-1})	205, 232
21	1260		5.0		1.23		419 p. 181
23	1200	12.4	6.0			2.4(@75 min^{-1})	205, 232
23	1260		5.0		1.46		419 p. 181
24	1260	15.9	∿5.3	20	1.62		417
24	2400	14.8	∿5.3	20	1.68		417
24	2320	15.9	∿5.3	20	1.62		417
24	2300	51(peak)	5.4		NA		307
25	1200	13.7	4.0			1.5(@75 min^{-1})	205, 232
25	1260		5-7.2		1.86		419 p 181
27	1260	16.1	∿5.3	20	1.61		417
*27	1260	∿13.3		20	1.77		309
27	1260		4.0			6.3(@50 min^{-1}) 4.0(@80 min^{-1}) 4.6(@110 min^{-1}) 3.5(@140 min^{-1})	237 237 237 237

*steady flow rate

6120) prostheses. The fact that the cloth covered models can see more hemolysis compared to the non-cloth covered models is highlighted in studies where both types of valves were investigated (36, 56, 97, 104, 120, 154, 163, 222, 295).

Hamby, et al., (452) in an excellent clinical study, demonstrated the hydrodynamic instability of the Starr-Edwards aortic ball valves in 41 patients. The study combined cineflouroscopy, phonocardiography and hemodynamic measurements. In 20 of the patients the poppet remained in a relatively fixed position (even though it rotated) at the apex of the cage during systolic ejection. In 11 patients the poppet bounced away from the apex of the cage during early ejection and promptly returned to the apex during the remainder of the ejection period. In 10 patients premature partial closure of the valve was observed during ejection. After striking the apex of the cage during early ejection the poppet descended almost half the distance toward the base of the valve and remained in a relatively fixed, partially closed position during the remainder of the ejection period. Instability of the poppets of the Starr-Edwards ball valves has also been observed in some of our patients at the USC-LA County Medical Center.

(c) In Vitro Results

The in vitro pressure drop studies indicate calculated VA's of 1.04 to 2.12 cm^2 for aortic and mitral valves in the 19 to 32 mm size range (Tables 9 and 10). As stated by Lefrak and Starr (412 p. 67) there is no difference in the in vitro pressure drop and regurgitant characteristics of the non-cloth covered (1200/1260, 6120) and the cloth covered (2310/2320, 2400, 6310/20, 6400) prostheses. The in vitro

STARR-EDWARDS BALL VALVE (continued)

HEMOLYSIS

Position	Model #	LDH	Hgb	Hapt	Other	Remarks	Ref#
A	2310-20	794 IU/L (<270)*	NA	NA		100 pts	104
A	2400	485 IU/L (<270)*	NA	NA		23 pts; model 2400 causes less hemolysis compared to models 2300-10-20	104
A	1000	162±22 units (23-75)*	NA	NA		most of 15 had mild hemolysis	36
A	1200	196±22 units (23-75)*	NA	NA		13/13 had mild hemolysis	36
A	1260	190±19 units (23-75)*	NA	NA		26/26 had mild hemolysis 1/26 had anemia	36
A	2300	574±87 units (23-75)*	NA	NA		28/46 had anemia 46/46 had mild hemolysis	36
A	2310	344±43 units (23-75)*	NA	NA		10/27 had anemia 27/27 had mild hemolysis	36
A	2320	325±37 units (23-75)*	NA	NA		9/29 had anemia 29/29 had mild hemolysis	36
A	2320	NA	NA	NA		135 pts; 24/135 had hemolytic anemia	96
A	cloth-covered	NA	NA	NA		12/14 had renal hemosiderosis	120
A	non-cloth-covered	NA	NA	NA		24/35 had renal hemosiderosis	120
NA	NA	NA	NA	NA		7/8 had anemia	143
A	2300-10	NA	NA	NA		increased osmotic fragility	155

*normal values

± SEM

HEMOLYSIS STARR-EDWARDS BALL VALVE (continued)

Position	Model #	LDH	Hgb	Hapt	Other	Remarks	Ref#
A	2300	2422±1790 IU/L	NA	NA		15/15 had moderate to severe hemolysis	161
A	2310	1280±776 IU/L	NA	NA		15/17 had moderate to severe hemolysis	161
A,M	2310-10-20 6300-10-20	NA	NA	NA		61/1187 had severe hemolysis; 5 required valve replacement	195
A	1000,1200 1260,2300	NA	NA	NA		19/302 had moderate hemolysis	60
A	2300	NA	NA	NA		severe hemolytic anemia in one patient due to cloth wear	74
A	2300	NA	NA	NA		15% of 28 had hemolytic anemia	80
A	2310	NA	NA	NA		6% of 38 had hemolytic anemia	80
A	1000	NA	NA	NA		7/90 had hemolytic anemia	95
A	2310-20	794 IU/L (<270)*	NA	NA		most of 123 had mild to moderate hemolysis	97
A	2400	485 IU/L (<270)*	NA	NA		23 pts had mild hemolysis	97
M	6310-20	210-480 units	NA	10.6-16.8 mg%	plasma Hgb 0.8-15.0 mg%	14 had mild to moderate hemolysis	98
A,M	1260,6120	NA	NA	NA		97 had mild hemolysis	154
A,M	2300,6300	NA	NA	NA		69 patients studied; significantly more hemolysis observed with cloth-covered models	154

± SEM

*normal values

results also indicate low regurgitant volumes for the Starr-Edwards ball valves.

There have been a number of flow visualization studies conducted on the Starr-Edwards ball valves in the aortic and mitral positions (169, 175, 199, 205, 211, 236, 304, 305, 310, 363, 416). Wieting (416) observed the flow patterns downstream from a 27 mm model 1260 ball valve, under pulsatile flow conditions. During systole he observed a large turbulent wake distal to the ball. He also found that the ball bounced at the apex of the cage and this probably increased size of the turbulent wake. The large amplitude bounces increased the relative velocity between the surface of the ball and the fluid flowing past it. Yoganathan et al., (417, 427) and Figliola (411) have also observed the poppet instability phenomena with the model 1260 valve.

As observed by Yoganathan, et al., in their studies, the instability of the poppet leads to larger pressure drops across the prosthesis. Dellsperger and Wieting (305) studied a model 6400 valve. In the mitral position they observed boundary layer separation resulting in a stagnation point at the apex and a toroidal vortex downstream from the valve during most of diastole. Smeloff, et al., (175) under pulsatile flow observed an area of stasis at the apex of the cage and a region of flow separation adjacent to the sewing ring. Wright and Temple studied flow patterns around a 24 mm aortic (model 2400) and a 32 mm mitral (model 6400) valves under pulsatile flow conditions. In the aortic position they observed a small disturbance extending about half the ball diameter immediately downstream from the apex of the cage. This region of flow gradually extended throughout systole until after

TABLE 12

THROMBOEMBOLIC COMPLICATIONS : STARR-EDWARDS BALL VALVE

Position	Model#	Patient Ratio	Rate % per pt-yr	Deaths	Anticoagulation	Remarks	Ref #
M	6300-10	6/67	NA	NA	Warfarin		48
A	2310	37 patients studied		7	NA	poppets held at apex of cage by thrombus & fibrin	58
A	2310	9%	NA	NA	none	early	54
A	2400			NA	none	thrombus on struts or ring	89
A	1200	9/95	NA	NA	all patients	3-TEC's early 6-TEC's late	60
A	1000	45/157	NA	9(late)	all patients	9-TEC's early	60
A	2300	0/34	NA	0	67% on anticoagulation		60
A,M	NA	NA	NA	NA	NA	reduced platelet adhesiveness	91
A,M, T&double	2300-10-20 6300-10-20	11/267	NA	2	coumadin		63
A	1000,1200 1260,2300,2320	11/29	NA	0	most on warfarin	platelet survival time shortened to 2.5 days (model 1000) 3.0 days(model 1200-60, 2300-20); from normal of 3.4 days	101
M	6120	NA	6.1±1.1	NA	all patients		99
M	6310-20	NA	3.0±.7	NA	all patients		99

± SEM

THROMBOEMBOLIC COMPLICATIONS : STARR-EDWARDS BALL VALVE (continued)

Position	Model#	Patient Ratio	Rate % per pt-yr	Deaths	Anticoagulation	Remarks	Ref #
M	6120	3%	NA	NA	most patients	164 patients studied 1 year post-op	104
M	6120	38%	NA	NA	most patients	64 patients studied 8 years post-op	104
M	NA	13 patients studied	-	-	none	platelet survival time 5.5 ± 23 days, normal 6.7 ± .2	106
A,M	2300,6300	23/153	NA	7	warfarin		107
A,M	NA	all observations on autopsy			49/71 on warfarin	71/96 had thrombus on mid-portion of struts & at apex of cage	120
A,M	NA	all observations at autopsy			7/17 on warfarin	17/20 valves had thrombus	121
A	2300	9/72	NA	1	none		67
A	2300-10-20	14/147	NA	2	all patients		100
A	2300-10-20	20/82	NA	1	none		100
A	2400-10	17/327	3.3 ± .8	3	all patients		70
M	6400-10	28/270	4.6 ± .9	0	all patients		70
A	2310	-	-	-	coumadin	fibrin deposits on inside of each strut -1 patient	72
A	2320	-	-	-	coumadin	severe cloth wear led to TEC, 1 pt.	90

± SEM

THROMBOEMBOLIC COMPLICATIONS ; STARR - EDWARDS BALL VALVE (continued)

Position	Model#	Patient Ratio	Rate % per pt-yr	Deaths	Anticoagulation	Remarks	Ref #
A	2310	1%	NA	NA	coumadin		250
A	2320	0%	0	0	coumadin		250
M	6000	61%	NA	NA	coumadin		250
M	6120	20%	NA	NA	coumadin		250
M	6300	27%	NA	0	coumadin		250
M	6310	8%	NA	NA	coumadin		250
M	6320	0%	0	0	coumadin		250
A,M	2300-10 6300-10	4%	NA	NA	warfarin or coumadin		243
M	6000	6/17	NA	NA	NA	platelet survial time shortened to 2.7±.17 days normal = 3.7±.04	242
A	2310	2/62	NA	0	warfarin		57
A,M	2300-10 6300-10	6/223(early) 6/118(late)		2(early) 2(late)	coumadin		61
A	1000	12/90	NA	NA	all patients		95
M	6000	27/65	NA	NA	all patients		95
A	1000,1200 1260	40/162	NA	17	all patients		266
M	6120	37/18	5.8 6.4(second embolous rate)	4	all patients	5 valves replaced at surgery due to thrombotic stenosis	445
A ± SEM	1200,1260	53/249	5.0 5.5 (second embolous rate)	2	all patients		445

the base of the three struts and extended about 2 to 5 mm downstream from the valve along the walls of the flow chamber. At a flow rate of 25 l/min the region of stasis was about 7 to 8 mm in size. Maximum wall shears measured were on the order of 1750 dynes/cm^2, and poppet wall shears were on the order of 2500 to 2800 dynes/cm^2. Turbulence intensity levels as high as 50% were measured in the wake region immediately downstream from the poppet, and in the annular region between the poppet surface. Maximum turbulent shear stresses on the order of 2000 to 5000 dynes/cm^2 (peak values) were measured in these regions.

(d) Correlation

The in vivo and in vitro pressure measurements indicate that like other ball valves, due to its centrally occluding design, the Starr-Edwards ball valves are moderately stenotic in the medium to larger sizes. In the smaller sizes the valves are very stenotic. Patients with this prosthesis would not be able to lead very strenuous life styles. The prosthesis does have low regurgitant volumes, the lowest among mechanical prostheses in current clinical use. The in vivo and in vitro data seem to indicate that the instability of the silicone rubber poppet (1200/1260, 6120) could lead to larger pressure drops across the prosthesis.

The large wall shear stresses created by the Starr-Edwards ball valves could cause lethal damage to the endothelial lining of the vessel wall adjacent to the valve, especially in the aortic position. The bulk turbulent shear stresses are large enough to cause sub-lethal and/or

mainly occurred on the inner aspects of the cage. The cloth covering along the inside of the orifice probably also causes flow separation, and if so could lead to excess tissue growth along the fabric in the orifice and cause the valve to become stenotic.

Sizes and Dimensions

Size	Sewing Ring Diameter(mm)	Strut Projection (mm)	Orifice Diameter(mm)	Primary Orifice Area(cm^2)
19	19	19.6	12.3	1.19
21	21	25.7	14.0	1.54
23	23	27.6	15.1	1.83
24	24	28.7	16.1	2.05
26	26	30.7	17.1	2.31
29	29	34.7	19.1	2.85
31	31	38.3	21.0	3.45
33	33	41.9	22.9	4.10
34	34	44.2	24.1	4.56

(b) In Vivo Results

Very little good clinical hemodynamic data exists on the Smeloff-Cutter valve (Tables 13 and 14), inspite of the fact the prosthesis has been in clinical use for almost 15 years. The little hemolysis data that exists on Smeloff-Cutter valve patients (Table 17) does also indicate instances when hemolytic anemia has occurred. Sensitive quantitative blood studies such as LDH and haptaglobin levels are sadly lacking in Smeloff-Cutter valve recipients. Thromboembolic data (Table 18) show that this prosthesis has TEC rates in the approximate range of 1.5 to 6.5% per pt. yr. Patients with mitral prosthesis have the higher TEC rates. Thrombus formation on the valve superstructure has been observed on recovered Smeloff-Cutter aortic and mitral valves (185, 263, 267, 268, 283, 284, 372, 439). In most cases thrombus formation has been found at the junctions of the downstream struts and the metal orifice ring. Thrombus has also occasionally been found at the same junctions on the upstream side. Smeloff-Cutter aortic ball valves recovered at the LA County-USC Medical Center (439) have in

TABLE 14

IN VIVO PRESSURE DROPS: SMELOFF-CUTTER MITRAL VALVE

Tissue Annulus Size mm	Rest					Exercise					ref#
	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	
NA	4	4.13		2.85	NA	4	7.7		3.13	NA	262

TABLE 15

IN VITRO PRESSURE DROPS: SMELOFF-CUTTER AORTIC VALVE

Tissue Annulus Diameter mm	Model #	$\bar{\Delta p}$ mmHg	CO ℓ/min	Q_{rms} ℓ/min	VA cm^2	RV cm^3/stroke	Ref #
24		12.7	∿5.3	20	1.81		417
24		37(peak)	5.6		NA		307
24		9.3	6.0			6.4 (@75 min^{-1})	205,232
26		11.8	∿5.3	20	1.88		417
*26		13.3		20	1.77		309
*26		∿ 9.5		20	2.09		177
26		12.8(peak)	3.24	21.4		9.3 (@72 min^{-1}) 8.2 (@78 min^{-1}) 11.0 (@55 min^{-1})	306 306 306

*steady flow data

his studies (304, 410) observed that the separated region behind the ball was relatively small. He also observed a very short-lived small vortex forming in the wake region during late systole. In addition, in his studies as the valve opened during systole the ball bounced several times against the downstream cage and finally settled on the fifth cage contact.

Yoganathan, et al., (353, 354, 417, 425) have made velocity and shear stress measurements immediately downstream from a size 26 Smeloff-Cutter aortic valve at steady flow rates of 10 and 25 l/min. At the high flow rate they measured wall shear stresses as high as 1670 dynes/cm^2 and estimated maximum turbulent shear stresses to be on the order of 1000 to 4000 dynes/cm^2. The flow field was found to be most turbulent in the annular region between the occluder and aortic walls and the wake region immediately downstream from the occluder and cage. Figliola, et al., (351, 411) have also made similar observations with a Starr-Edwards 1260 ball valve. Yoganathan, et al., also observed that there was no region of stagnation near the apex of the downstream cage. Instead, negative velocities on the order of -10 to -20 cm/s were observed creating a washing effect at the apex of the cage. Regions of flow separation were observed adjacent to the sewing ring and near the base of the aortic side from the cage struts, along the downstream struts and immediately downstream of the ball (i.e.: wake region), similar to those observed by Figliola,et al., with the Starr-Edwards ball valve (351, 411). Hwang, et al., (419 p. 91) have made preliminary velocity and shear stress measurements downstream from a size 26 aortic valve under pulsatile flow conditions. The measurements

were made about 40 mm downstream from the valve sewing ring at a cardiac output of 4.2 l/min. They measured a maximum turbulent shear stress of about 320 dynes/cm^2. This value seems low and is probably due to the fact that the measurements were made only 40 mm downstream from the valve and not any closer. Since the laser-Doppler anemometer was not able to measure flow directionality they were not able to observe any regions of flow separation.

(d) Correlation

The in vivo and in vitro pressure measurements indicate that the Smeloff valve is stenotic because of its centrally occluding design characteristics. The wall shear stresses, like for other peripheral flow prostheses, are elevated and could cause damage to the endothelial lining of the vessel walls adjacent to the valve. The problem would be most severe in the aortic position because of the proximity of vessel wall surfaces to the prosthesis (i.e., the region between the wall surfaces and poppet surfaces are narrow, compared to that present in the ventricle for the mitral valve). Roberts, et al., in their pathologic studies of ball and disc type valves observed damage to the endothelial lining of the vessel wall (mostly aortic) adjacent to the prosthesis (116, 117, 119-112). The damage causes intimal proliferation of fibrotic tissue on the vessel wall. On rare occasions this intimal proliferation in the aortic position may extend into one or both coronary arteries and cause sudden death. Roberts states (116) that it is likely that this intimal proliferation will progressively increase with time.

THROMBOEMBOLIC COMPLICATIONS : SMELOFF-CUTTER BALL VALVE (continued)

Position	Model#	Patient Ratio	Rate % per pt-yr	Deaths	Anticoagulation	Remarks	Ref #
A		4/358	2.9	NA	aspirin and dipyridamol		285
A		4/358	5.4	NA	none		285
M		1.2%	NA	0	all patients		54
M		3/27	NA	3	NA		54
A		3/33	NA	0	warfarin	thrombus formation on 2/21 recovered valves	284
M		13/56	NA	2	NA	2 thrombosed valves caused death	263

4.

BRAUNWALD-CUTTER BALL VALVE

(a) Valve Description

The Braunwald-Cutter prosthesis is an open cage ball valve. The entire valve housing is machined from a single piece of titanium, and is completely covered with cloth. The orifice cloth is made of polypropylene while the struts are covered with knitted Dacron tubing. The poppet is made of silicone rubber and is housed within a three strut cage. The valve has been used in both the aortic and mitral positions since 1968. The clinical use of the valve was discontinued around 1975.

Sizes and Dimensions

Size	Sewing Ring Diameter(mm)	Orifice Diameter (mm)	Primary Orifice Area(cm^2)
A20	20	12.4	1.21
A22	22	14.4	1.62
A23	23	15.2	1.82
A24	24	16.0	2.01
A25	24	17.7	2.45
A27	25	18.6	2.72
A29	29	20.2	3.21
M26	26	15.2	1.81
M28	28	16.8	2.22
M30	30	18.4	2.66
M32	32	20.0	3.14
M34	34	21.2	3.53

TABLE 20

IN VIVO PRESSURE DROPS: BRAUNWALD-CUTTER MITRAL VALVE

Tissue Annulus Size mm	Rest N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	Exercise N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	ref#
30	1	6.7		4.4	2.32						359
32	3	4.6 (3.5-5.0)		2.8 (2.2-3.4)	2.74 (1.92-3.21)						359
34	4	4.5 (1.9-8.0)		2.7 (2.3-3.3)	2.72 (2.26-3.46)						359
32 & 34	6	8.3±1.1*		2.5±0.2*	1.6±0.1*	6	18.1±1.3*		4.3±0.3*	1.7±0.1*	18

*±SEM

TABLE 21

IN VITRO PRESSURE DROPS: BRAUNWALD-CUTTER AORTIC VALVE

Tissue Annulus Diameter mm	Model #	$\overline{\Delta p}$ mmHg	CO ℓ/min	Q_{rms} ℓ/min	VA cm^2	RV cm^3/stroke	Ref #
*23		∿ 37.0		20	∿ 1.06		84

*from steady flow data

TABLE 23

HEMOLYSIS

BRAUNWALD-CUTTER BALL VALVE

Position	Model #	LDH	Hgb	Hapt	Other	Remarks	Ref#
A		NA	NA	NA		3/77 had anemia	54
A,M		NA	NA	NA		9/243 had anemia	191
A		NA	NA	NA		3/3 had severe hemolysis due to cloth wear	76
M		elevated levels	NA	normal		10 pts. studied, all had mild hemolysis	18

(c) In Vitro Results

As can be seen from Tables 21 & 22 in vitro fluid dynamic data on the Braunwald-Cutter valve in the open literature is non-existent. No flow visualization studies on this valve exist. It is our opinion that velocity profiles would be similar to those obtained with the Starr-Edwards and Smeloff-Cutter valves.

(d) Correlation

The Braunwald-Cutter prosthesis like other ball valves is stenotic. Patients with this valve would have to lead a rather low-profile life style. If the assumptions made in the in vitro section are correct, the wall shear stresses created by this valve could also lead to endothelial damage of the vessel walls adjacent to the prosthesis. The turbulent shear stresses could cause sub-lethal and/or lethal damage to red cells and platelets. Such shear damage could lead to hemolytic and thromboembolic problems. Red cells and platelets would also have reduced half-lifes. Thrombus formation and tissue overgrowth could occur at the base of the struts due to the flow separation at those locations. Therefore the thromboembolic and mild hemolytic problems observed with this valve may be directly related to its predicted fluid dynamic characteristics.

TABLE 25

IN VIVO PRESSURE DROPS: KAY-SHILEY MITRAL VALVE

Tissue Annulus Size mm	Rest N	Rest MG mmHg	Rest PG mmHg	Rest CI ℓ-min^{-1}/m^2	Rest VA cm^2	Exercise N	Exercise MG mmHg	Exercise PG mmHg	Exercise CI ℓ-min^{-1}/m^2	Exercise VA_2 cm^2	ref#
Series K+T											
28	1	13		1.97	NA						225
	1	9		4.7(CO)	0.9						164
30	5	9.6 (5-15)		2.88 (1.8-4.7)	NA						225
31	6	9.6 (0-22)		2.78 (2.05-3.22)	NA						225
33	1	30		1.37	NA						225
MG Series											
27	1	14		4.0(CO)	1.0						164
31	7	6.6 (4-10)		3.9(CO) (2.7-5.6)	1.3 (0.9-2.0)						164
33	5	4.6 (3-7)		4.4(CO) (3.8-5.4)	2.1 (1.2-2.6)						164

(b) In Vivo Results

The Kay-Shiley mitral valve had calculated VA's of 0.9 to 2.1 cm^2 in the 28 to 33 mm size range (Table 25). These results indicate this prosthesis was more stenotic than the caged ball type valves. As Table 27 indicates there are very few articles on hemolysis with the Kay-Shiley valve. The valve did not seem to cause clinically significant hemolysis, but probably caused mild hemolysis. One of the major problems with this prosthesis was, however, thromboembolic complications, as clearly shown by the data in Table 28. TEC rates as high as 34.4% per pt. yr. have been observed with this prosthesis. Thrombus formation on the valve superstructure causing dysfunction of the Kay-Shiley valve is well documented in the literature (30, 116, 119, 120, 166, 167, 215, 224, 226, 227, 263, 370, 372, 419, p. 385). Thrombi were mainly located at the junction of the cage struts with the metal orifice ring, up the vertical struts for variable distances, and occasionally completely covering the entire metal superstructure. Clots have also been observed on the disc and on the sewing ring. The prosthesis has occasionally been completely occluded by thrombotic material.

Excess tissue growth on the sewing ring has also been a problem with this prosthesis (103, 164, 224, 225, 372, 414 p. 598, 419 p. 385). In some cases the movement of the disc was severely restricted because of tissue overgrowth between the disc and sewing ring. In other cases part of the disc has been trapped by tissue overgrowth and thrombus formation. Such entrapment has transformed the disc into a

hinged mechanism, thereby reducing the flow orifice, as well as leading to accelerated edge wear of the disc by the metal struts (412 p. 177). Excess tissue growth along the sewing ring have on occasions impaired the rotation of the disc. This impairment has led to grooving of the downstream face of the disc from mechanical contact with the horizontal struts (164, 372, 439).

(c) In Vitro Results

Very few in vitro studies exist on the Kay-Shiley valve. Weiting has observed the flow patterns around a 28mm Kay-Shiley valve in an aortic chamber (416). He observed a symmetrical toroidal vortex and a wake downstream from the disc caused by boundary layer separation during systole. He also observed an area of stasis at the center of the distal surface of the disc. The flow was jet like in the regions between the disc and the flow channel walls. Similar flow visualization studies and observations have been made by Duff (410). Figliola (351, 411) has made velocity and shear stress measurements downstream from a 27 mm Kay-Shiley valve (T series) in an aortic chamber under steady flow conditions. He observed a jet type flow between the poppet and flow chamber wall. He also observed flow separation at the sewing ring, and at the junction of the vertical struts and the orifice ring. A large wake with recirculating flow was monitored downstream from the face of the disc. At a flow rate of 25 l/min he measured a maximum wall shear stress of 2548 dynes/cm^2, turbulence intensities of 48% and Reynolds shear stresses of 800 dynes/cm^2. He also was able to measure shear stress of about 775 dynes/cm^2 at the occluder wall surface. The

THROMBOEMBOLIC COMPLICATIONS : KAY-SHILEY DISC VALVE (continued)

Position	Model#	Patient Ratio	% Rate per pt. yr.	Deaths	Anticoagulation	Remarks	Ref #
M	T	2/23	NA	NA	all patients		226
M	MG	0/14	-	0	all patients		226
M	DMG	0/4	-	0	all patients		226
A	K&T	3/60	NA	1	anticoagulation discontinued in 3 pts.	death due to thrombosed valve	227
M	K&T	33/69	29.6	15	warfarin		370
M	NA	3patients	-	-	none	3 patients-platelet survival time shortened to 5.5± .23 days (6.7±.2)*	106

* normal values

± SEM

junctions of the vertical struts and orifice ring and near the sewing ring could lead to thrombus formation and tissue overgrowth at these locations. As stated previously clinical pathalogic findings indicate that these regions are the most prone to thrombus formation and tissue overgrowth with this valve. In addition, Roberts (116, 117) states that intimal proliferation of the vessel wall adjacent to valve (mainly in the aortic position) is probably most severe with the disc type valves. The intimal proliferation is caused by large wall shear stresses.

TABLE 29

IN VIVO PRESSURE DROPS: BEAL MITRAL VALVE

Tissue Annulus Size mm	Rest N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	Exercise N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	ref#
Small 31.7	1	NA		NA	1.6						40
Medium (model 104&105)	8	7.9 (0-16)		NA	1.4 (1.1-1.6)						38
	6	NA		NA	1.5						40
Large (model #104)	6	6.4 (3.5-10)		NA	2.3 (1.3-3.3)						38
	10	NA		NA	1.7						40
Large=7 Med. =14 Sm. =2	23	7.5±1.6 * (0-16)		3.39±0.4 * (1.6-6.2)	NA	20	12.5±2.3 * (2-25)		4.7±0.2 * (2.3-9.0)	NA	39
Teflon models											
Small	7	15.2 (4.9-23.3)		3.28 (1.70-3.92)	1.43 (0.79-1.7)	5	24.9 (20.0-28.4)		3.63 (2.03-4.02)	NA	148
Medium	13	10.4 (4.2-14.9)		2.33 (1.87-3.12)	1.56 (0.62-2.58)	10	25.3 (21.4-39.7)		3.85 (2.81-4.97)	NA	148
Large	4	9.5 (8.0-12.8)		2.74 (2.15-3.06)	1.58 (1.50-1.73)	4	18.6 (13.0-25.4)		3.31 (2.39-4.32)	NA	148

* ±SEM

(b) In vivo Results

The clinical pressure drop results obtained with the Beall valve indicate that it is even more stenotic than the Kay-Shiley disc valve (Table 29). Calculated VA's varied between 1.4 and 2.3 cm^2 for valve sizes in the 31 to 41 mm range. As shown by the data in Table 31 one of the major clinical problems with the Beall disc valve was the amount of hemolysis it caused. It has been suggested that the Dacron velour cloth covering used was the reason for the excessive hemolysis observed with this valve (412 p. 180). It has also been suggested that disc wear of the Teflon disc models exacerbated the native hemolysis of this prosthesis (142). Nearly all patients who had this valve suffered at least mild intravascular hemolysis. A comparison of the "patient ratio" columns in Tables 28 and 32 tends to indicate that with anticoagulation therapy, thromboembolic complications with the Beall valve were not as severe as those observed with the Kay-Shiley valve. But as stated by Lefrak and Starr (412 p. 181) only a few publications have appeared in which time-related analysis has been utilized to analyze the rate of postoperative thromboemboli. Thrombus formation causing valve dysfunction has also been documented (38, 40, 142, 146, 190, 215). As stated by Roberts, et al., (117) disc type prosthses will develop thrombotic material at the junctions of the vertical struts and the orifice ring, along the vertical struts and across the face of the disc. Usually the amount of thrombus on the struts or primary orifice is not sufficient to interfere with the proper movement of the disc, and clinical evidence of systemic embolic incidents are infrequent when the prosthetic thrombi are small. Large thrombi may, however, obstruct flow

through the prosthesis and may immobilize the disc. They also state that prostheses of the disc type may be tilted in the cage by thrombus on one side, or thrombus may fill the entire space between the disc and the ring, causing complete immobility of the poppet (117). As observed with the Kay-Shiley valve the thrombus formation may cause improper motion of the disc (proper motion requiring movement up and down the cage, and rotation), thereby leading to grooving and notching of the disc (149, 150, 418 p. 463).

(c) In Vitro Results

In vitro fluid dynamic studies on the Beall disc valve are virtually non-existent in the open literature. It is doubtful if any such tests were even performed by the valve manufacturer when the valves were released in the mid to late 1960's. It is, however, our opinion that the velocity and shear fields downstream from this valve are similar to those observed with the Kay-Shiley and Starr-Edwards disc valves.

(d) Correlation

The Beall disc valve is a very stenotic valve design. If the assumptions about its in vitro fluid dynamic characteristics are correct, the wall and turbulent shear stress created by this valve could easily damage the endothelial lining of the vessel walls, and cause sub-lethal and/or lethal damage to blood elements, respectively. In addition, if the red cells were to attach themselves to the Dacron velour cloth covering, the shear stresses adjacent to the valve

superstructure would be more than sufficient to cause lethal red cell damage (hemolysis) as observed clinically with this prosthesis and the cloth covered Starr-Edwards ball valves. The region of flow stasis adjacent to the downstream face of the disc and the regions of flow separation at the junctions of the vertical struts and the orifice ring could lead to a buildup of thrombotic material at those locations as has been observed on some recovered Beall valves. The early model Beall valve was briefly utilized in the aortic position but its use in this location was abandoned because of obstructive, thrombogenic and wear characteristics (116, 117). Furthermore, Roberts in his pathologic studies observed that disc valves in the aortic position cause intimal proliferation of the aortic root, as a result of excessive wall shear stresses (116, 117).

modified valve was designed according to Dr. Bjork to improve the conventional Bjork-Shiley valve in three respects: (1) provide increased strength of the valve by making the inlet strut an integral part of the orifice ring and doubling its cross-sectional area (2) improve the hydrodynamics (3) reduction in the area of low flow and stagnation behind the disc. The design change includes the convexo-concave configuration of the disc and a pivot point which has been moved several millimeters downstream so that the disc in the open position is moved further out of the orifice ring.

Valves manufactured after September 1975 have a radio-opaque tantalum loop incorporated in the pyrolytic carbon disc to allow evaluation of the opening angle of the disc.

Sizes and Dimensions

Size	Sewing Ring Diameter(mm)	Orifice Diameter (mm)	Primary Orifice Area (cm^2)
17	17	12	1.0
19	19	14	1.5
21	21	16	2.0
23	23	18	2.5
25	25	20	3.2
27	27	22	3.8
29	29	24	4.5
31	31	24	4.6

TABLE 34

IN VIVO PRESSURE DROPS: BJORK-SHILEY (CONVEXO-CONCAVE) AORTIC VALVE

Tissue Annulus Size mm	Rest N	MG mmHg	PG mmHg	AVF ℓ-min^{-1}	VA cm^2	Exercise N	MG mmHg	PG mmHg	AVF ℓ-min^{-1}	VA cm^2	ref#
21	10	16.2±8.1**		14.7±3.4**	1.41±.21**	6	20.7±7.9**		17.7±3.8**	1.51±.32**	2
23	10	14.9±6.0**		16.4±5.0**	1.67±.22**	7	18.6±6.3**		19.4±4.1**	1.67±.27**	2
27&28	8		6.2±2.8**	5.9±1.1** (CO)	2.56±0.71**	8		4.2±1.8**	8.5±1.3 (CO)	1.3±0.4**	393

** ± SD

(b) In Vivo Results

Clinical hemodynamic results indicate that the Bjork-Shiley valve has improved pressure drop characteristics compared to the centrally occluding (ball and disc) and porcine valve prostheses. Calculated valve areas varied from 1.06 to 2.56 cm^2 for aortic valve sizes of 19 to 31 mm, and 1.8 to 2.6 cm^2 for mitral valve sizes of 27 and 29 mm (Tables 33-35). The limited hemodynamic data tend to indicate no significant differences in the pressure drop characteristics of the spherical and convexo-concave disc aortic valves. Due to its world wide popularity there is a large amount of literature in the medical field on this prosthesis. Hemolysis data presented in Table 38 indicate that the Bjork-Shiley prosthesis can cause mild to moderate hemolysis. Patients with this prosthesis, however, rarely develop anemia because the body usually compensates adequately for the hemolysis caused by the valve. As shown in Table 39 the prosthesis has a TEC rate of about 4 to 6% per pt. yr. The major problem with the Bjork-Shiley valve is its potential to thrombose, sometimes catastrophically, especially in patients not on anticoagulation therapy (11, 13, 22, 23, 41, 45, 46, 47, 52, 53, 110, 118, 44, 193, 197, 215, 277, 371, 392, 401, 419 p. 385, 446, 448). In addition to thrombus formation, excess tissue overgrowth has also been observed on recovered Bjork-Shiley valves. Please note that the above references all pertain to the standard (ie: spherical disc) Bjork-Shiley model (except ref 11, 41). There have been no long term studies on the convexo-concave model, and thrombus formation on this model has so far only been reported in two articles (11, 41). Thrombus formation mainly occurs on the outflow face of the disc especially in the well, and along

IN VITRO PRESSURE DROPS: BJORK-SHILEY AORTIC VALVE (CONTINUED)

Tissue Annulus Diameter mm	Model #	$\bar{\Delta p}$ mmHg	CO ℓ/min	Q_{rms} ℓ/min	VA cm^2	RV cm^3/stroke	Ref #
*27	C.C.	6.4		20	2.55		203
27	std.	11.9(peak)	3.14	22.8(peak)	N/A	15.1 (@72 min^{-1})	306
						10.9 (@78 min^{-1})	306
						20.8 (@55 min^{-1})	306
*27	std.	∿6.2		20	2.59		177
27	std.	4.0				15.3 (@50 min^{-1})	237
		4.0				10.6 (@80 min^{-1})	237
		4.0				8.7 (@110 min^{-1})	237
		4.0				7.4 (@140 min^{-1})	237
27	C.C.	4.0				13.0 (@50 min^{-1})	237
		4.0				10.5 (@80 min^{-1})	237
		4.0				7.8 (@110 min^{-1})	237
		4.0				6.0 (@140 min^{-1})	237

*steady flow data

the struts in the minor outflow region. However, thrombus formation on both the inflow and outflow faces of the disc has been observed in some recovered valves. Excess tissue overgrowth is observed mainly along the sewing ring of the minor outflow region. The amounts of thrombus formation and/or tissue overgrowth observed on recovered Bjork-Shiley aortic and mitral valves has varied from total valve occlusion to a thin layer. In some instances the combination of thrombus formation and tissue overgrowth has grown in such a manner to impede the complete opening of the tilting disc. In other instances, the disc has been found to be held immobilized in an open position by the vegetation. Therefore, it is of utmost importance that the physician be able to monitor the motion of the disc using cinefluoroscopy.

(c) In Vitro Results

The in vitro pressure drop results indicate (Tables 36 & 37) that the Bjork-Shiley valves have calculated VA's of 1.37 to 3.40 cm^2 for aortic and mitral valves in the 21 to 31 mm size range. There does not seem to be any significant difference in the pressure drop and regurgitation characteristics between the spherical and convexo-concave disc valves. Regurgitation data tend to indicate that at low heart rates and low cardiac outputs the Bjork-Shiley valve does have a significant regurgitant volume.

There have been many flow visualization studies conducted on the Bjork-Shiley valve in both the aortic and mitral positions (7, 49, 52, 141, 179 180, 199, 205, 211, 227, 232, 236, 305). Wright has studied the valve (size 25 mm) under pulsatile flow in a curved aorta (180,

Position	Model #	LDH	Hgb	Hapt	Other	Remarks	Ref#
M	std	425.5±124.8 U/L (150-450)*	14.32±1.34 g% (13.5-18.0)*	31.0 mg/dl (30-180)*		85% of 33 had hemolysis	198
A	NA	234 IU/L (range 178-287) (90-215)*	14.5 g/100 ml (range 13.1-16) (12.5-18)*	96 mg/dl (range 15-284) (170-300)*		7/10 had chronic hemolysis	218
double	NA	> normal	NA	reduced or absent		14/16 patients had hemolysis	220
A	std	195 U/L (131)*	15.1 g% (14.9)*	NA		74 had mild to moderate hemolysis	222
M		199±52 U/L	normal	18/40 <normal	plasma hgb 5 mg% (0 mg%)*	12/40 had increased LDH levels	391
M	std	NA	NA	NA		42% had hemolysis	295
double	std	NA	NA	NA		85% of 38 had increased LDH	420
A,M	std	510 U/L (452)*	NA	reduced in 10, absent in 3		13/16 had hemolysis	105
A,M	C-C	NA	NA	NA		37/37 had mild hemolysis	1
A	std	362 units (range 190-1080) (100-350)*	NA	37 mg% (range 4-164) (30-190)*	plasma hgb 57 mg% (11-15)*	LDH increased in most; hapt normal in half of the 60 pts studied	7

*normal values
± SEM

TABLE 39

THROMBOEMBOLIC COMPLICATIONS : BJORK-SHILEY TILTING DISC VALVE

Position	Model#	Patient Ratio	Rate % per pt-yr	Deaths	Anticoagulation	Remarks	Ref #
double	both	15/164	3.7	6	dicoumarol	11 TEC's due to inadequate anticoagulation; 5 thrombosed valves	41
double	std	1/25	1.0	1	dicoumarol	1 thrombosed valve due to discontinuation of anticoagulation	41
double	C-C	NA	0.9	NA	dicoumarol	1 thrombosed valve	41
A	std	5/106	NA	NA	warfrin		48
A	std	NA	NA	2	all patients	7/121 had large thrombi on struts and disc; only 1/7 had adequate anticoagulation	47
M	std	13/72	NA	16	discoumarol	majority of the 16 deaths were due to TEC's	42
A,M	std	25 patients	NA	2	heparin and coumadin	2/25 had massive thrombus across minor orifice causing death	45
M	std	8/81	NA	NA	all patients		21
M	std	5/109	NA	0	warfarin		54
A	std	8/77	5.6	3	all patients	2 thrombosed valves	53
M	std	12/127	NA	3	NA	deaths caused by thrombosed valves	52
double	std	2/23	8.2	0	warfarin		105

THROMBOEMBOLIC COMPLICATIONS : BJORK-SHILEY TITLTING DISC VALVE (continued)

Position	Model#	Patient Ratio	Rate % per pt-yr	Deaths	Anticoagulation	Remarks	Ref #
A,M & double	std. & C.C.					10 years experience 30/1800 valves had thrombotic occlusion	11
M	std.	NA	4.4	0.4%/pt-yr	NA	193 patients	11
M	C.C.	NA	1.2	0	NA	98 patients	11
M	std.	5/42	NA	1	all patients	1 thrombosed valve caused death	18
A	std.	2/57	NA	0	all patients		8
A	std.	36/379	NA	5	coumadin	in addition there were 8 thombosed valves; 7 caused deaths	401
M	std.	17/167	NA	4	coumadin	in addition there were 3 thrombosed valves; 2 caused deaths	401
double	std.	12/97	NA	0	coumadin	in addition there were 5 thrombosed valves; 4 caused deaths	401
A,M & double	std.	30/435	1.8	16	warfrin	13 valves were thrombosed; 11 caused death; 5/13 pts had discontinued warfrin	446

conducted at a steady flow rate of 25 l/min, (277, 352, 353, 417, 20). The measurements with the spherical disc valve identified a zone of stagnation about 20 mm wide near the aortic face of the disc. The average velocities in the major and minor outflow regions were around 100 and 25 cm/s, respectively, and the corresponding peak shear stresses adjacent to the sewing ring were approximately 700 and 150 dynes/cm^2. A maximum wall shear stress of 1390 dynes/cm^2 was measured. With the convexo-concave valve the region of stagnation was observed to be 10 mm wide, and the average velocities in the major and minor outflow regions were around 90 and 40 cm/sec, respectively. Peak shear stresses on surfaces adjacent to the sewing ring in the major and minor outflow regions were about 500-600 and 300-350 dynes/cm^2, respectively. The convexo-concave valve does, however, direct relatively high flow from the major outflow region towards one of the sinuses of Valsalva depending on its orientation. Wall shear stresses on the order of 1750 dynes/cm^2 were observed on the sinus wall towards which the high flow was directed. Turbulent measurements with both models indicated turbulent shear stresses on the order of 500 to 2000 dynes/cm^2 immediately downstream (3 to 15 mm) from the valve.

(d) Correlation

The in vivo and in vitro pressure measurements indicate that in the larger sizes and under resting conditions the pressure drop characteristics of the Bjork-Shiley valve are quite satisfactory. However, under exercise conditions and/or in the smaller sizes the valve could become mild to moderately stenotic. This is especially true in

along the sewing ring in that region. As has been observed in the recovered valves, the combination of thrombus formation and tissue overgrowth can produce catastrophic results.

The smaller region of stagnation, and the better distribution of flow between the major and minor orifices observed with the convexo-concave valve, may hopefully reduce the problems of thrombus formation on the outflow face of the disc, and excess tissue growth along the sewing ring of the minor orifice region.

IN VIVO PRESSURE DROPS: LILLEHEI-KASTER AORTIC VALVE

Tissue Annulus Size mm	Rest N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	Exercise N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	ref#
21	5	41 (13-64)	NA	2.4 (1.3-3.5)	0.77 (.67-.89)	2	75 (74-75)		5.11 (5.09-5.12)	.92 (.84-.99)	287
	2	30 (28-32)	NA	2.7 (2.6-3.1)	0.94 (.91-.97)						294
	11	NA	46 (28-70)	NA	0.81						125
	9	NA	45 (27-70)	NA	0.8 (0.5-1.1)						77
	5	47.6±12.7**	36±17.4**	NA	0.69±.13** (N=4)						16
23	3	31 (22-41)	NA	2.98 (2.9-3.1)	1.05 (.82-1.2)	3	52 (42-63)		6.56 (5.86-7.03)	1.25 (1.18-1.31)	287
	10	33 (16-53)	NA	3.5 (2.6-5.6)	1.21 (.83-1.56)						294
	16	NA	25	NA	1.10						125
	2	NA	32	NA	0.98						291
	12	NA	28 (5-57)	NA	1.1						77
	7	36.3±14**	29.3+20**	NA	1.17±0.14** (N=4)						16
25	3	17 (7-25)	NA	3.04 (2.2-4.8)	1.50 (1.10-1.75)	2	32 (27-38)		5.54 (3.4-7.7)	1.02 (1.07-1.9)	287
	3	22 (19-25)	NA	3.6 (3.3-4.0)	1.56 (1.36-1.68)						294
	11	NA	18	NA	1.20						125
	1	NA	12	NA	1.1						291
	15	NA	22 (10-42)	NA	1.3 (0.9-1.8)						77
	3	33±13.3**	12.0±5.9**	NA	1.98 (N=1)						16

** ± SD

TABLE 41a

IN VIVO PRESSURE DROPS: LILLEHEI-KASTER MITRAL VALVE

Tissue Annulus Size mm	Rest N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	Exercise N	MG mmHg	PG mmHg	CO ℓ-min^{-1}	VA$_2$ cm^2	ref#
23	2	9±4.2 **		NA	1.45±.07						291
	1	21		4.95	1.08						293
25	1	NA		NA	1.1						77
	2	7 (6-8)		1.62 (1.32-1.91)	1.39	1				1.12	293
27	9	8.33±5.2 **		NA	1.81±.81						291
	8	8 (4-14)		NA	1.6 (1-2.3)						77
	4	7.5 (4-13)		2.38 (2.06-2.63)	1.59 (1.56-1.63)	1	18		4.0	1.77	293
	2	10.1 (7.6-12.5)		2.9 (2.4-3.3)	1.8 (1.61-1.98)						294
29	7	6.57±2.7**		NA	1.87±.42						291
	14	7 (3-11)		NA	1.8 (1.0-2.8)						77
	1	6.5		4.11	2.13						293
	4	5.9 (6-10)		3.1 (2.4-3.0)	1.9 (1.56-2.19)						294
32	7	7±3.2 **		NA	2.33±.74						291
	2	5 (3-7)		NA	2.7 (2.6-2.7)						77
	3	4.3 (3.5-5)		3.5 (2.8-4.1)	3.02 (2.74-3.44)	1	14		3.8	2.89	293

** ±SD

Table 41b*

Comparison of In Vivo valve areas of Bjork-Shiley and Lillehei-Kaster mitral valves.

Name of Valve	Tissue Annulus Size mm	N	VA cm^2
Lillehei-Kaster	27	23	1.70
Lillehei-Kaster	29	26	1.85
Bjork-Shiley	27 & 29	63	2.24

*obtained from data presented in Tables 35 and 41a.

TABLE 42

IN VITRO PRESSURE DROPS: LILLEHEI-KASTER AORTIC VALVE

Tissue Annulus Diameter mm	Model #	$\overline{\Delta p}$ mmHg	CO ℓ/min	Q_{rms} ℓ/min	VA cm^2	RV cm^3/stroke	Ref #
19			5-7.2		0.85		419 p. 181
21		34.5(peak)	3.5		N/A		307
21			5-7.2		1.19		419 p. 181
23		28.0(peak)	4.3		N/A		307
23			5-7.2		1.57		419 p. 181
25		30.0(peak)	5.5		N/A		307
25			5-7.2		2.00		419 p. 181
*27		~ 4.1		20	3.18		177
27			5-7.2		2.49		419 p. 181
27.5		25.0(peak)	6.0		N/A		307

*steady flow data

death. Thrombosed valves have been recovered from both aortic and mitral positions. Thrombus formation mainly occurs on the outflow face of the disc. Thrombosis on both downstream and upstream faces has also been occasionally observed. In some instances the thrombus has formed in such a manner that the disc opening angle has been reduced. In other instances, the thrombus has frozen the disc in an open position. Problems of tissue overgrowth have not been specifically mentioned but it seems to occur together with thrombosis along the downstream sewing ring of the minor orifice region.

(c) In Vitro Results

Tables 42 and 43 indicate that the Lillehei-Kaster valve has reasonable in vitro pressure drop characteristics especially in the moderate to larger valve sizes. Calculated valve areas ranged from 0.85 to 3.94 cm^2 for the size 19 to 33 mm aortic and mitral valves. A study conducted on 30 mm Lillehei-Kaster and 29 mm Bjork-Shiley mitral valves tends to indicate that these valve designs have similar regurgitation characteristics (413).

Flow visualization studies have been conducted under pulsatile flow conditions in both aortic and mitral chambers (199, 211, 236, 305). Wright and Temple conducted their studies in a curved aorta (199). When the valve (25 mm size) was placed so as to open towards the inside of the aortic curve, about 100 ms into systole a small jet was formed which flowed tangential to the inside curve of the aorta. When the valve was oriented towards the outer curve of the aorta, clockwise circulating vortices were set up 4.5 cm distal to the valve. In addition a narrow

jet formed in the aortic curve. In this orientation the flow through the major orifice impinged onto the aortic wall and flowed along the wall. In the mitral position (29 mm valve size) a large, two dimensional vortex formed which dominated the left ventricle and may have aided valve closure. In this study it was noted that the flow patterns produced by the Lillehei-Kaster and Bjork-Shiley valves were quite similar. Dellsperger and Wieting (305) observed a region of stagnation underneath the downstream face of the disc with a 29 mm Lillehei-Kaster valve (mitral), during a major portion of diastole. A careful study should indicate similar qualitative findings in the aortic position during systole, as observed with the Bjork-Shiley aortic valve.

Using hot-film shear probes Tillman has measured "wall" (ie: surface) shear stresses along the metal orifice ring in the major and minor orifices (365). The experiments were conducted under pulsatile flow conditions in the aortic position. He observed peak shear stresses of 120 and 40 dynes/cm^2 in the major and minor orifices, respectively, during systole. Hwang, et al., (419 p. 91) have made velocity and shear stress measurements about 40 mm downstream from a 27 mm aortic valve a cardiac output of 3.8 l/min. These measurements indicated a peak turbulent shear stress of about 175 dynes/cm^2. If measurements were made closer to the valve, it is expected that the turbulent shear stresses measured would be on the order of 500 to 2,000 dynes/cm^2, as observed with the Bjork-Shiley valve (277, 351, 352, 411, 417). Since the flow field created by the Lillehei-Kaster valve is quite similar to that created by the Bjork-Shiley valve, it is expected that it will produce wall shear stresses of about the same magnitude [700 to 1400

dynes/cm^2 (411, 417)].

(d) Correlation

The in vivo and in vitro pressure measurements for this prosthesis do not predict the results. The in vivo hemodynamics indicate that the Lillehei-Kaster prosthesis is moderately stenotic in the medium and large sizes and very stenotic in the small sizes; results are comparable to those observed with the Starr-Edwards ball valves. The in vitro results indicate that the pressure drop characteristics of this prosthesis are quite similar to those observed with the Bjork-Shiley prosthesis. The most probable reason for this result is the observed clinical finding that the Lillehei-Kaster prosthesis does not open completely in vivo, while it does so in vitro in pulse duplicator systems. This performance is probably due to some complex "aerodynamic" lift phenomena occurring in the in vivo situation which we are at present unable to simulate in vitro. Sabbah and Stein have shown that at cardiac outputs of less than about 1 to 2 l/min with the valve oriented to open against gravitational forces, less than full opening is observed with the Lillehei-Kaster and Bjork-Shiley valves (208). No such effect is seen when the valve is oriented to open with gravity.

Flow visualization studies and the limited velocity and shear stress measurements indicate that sub-lethal and/or lethal damage could occur to the endothelial lining of the vessel wall, red cells and platelets. Therefore, hemolytic and thromboembolic problems are predictable with this prosthesis. In vivo and in vitro studies show that most of the flow through the valve occurs through the major outflow

9.

HANCOCK PORCINE VALVE BIOPROSTHESIS

(a) Valve Description

The Hancock porcine bioprosthesis, prepared by the Stabilized Glutaraldehyde Process ("SGP") has been in clinical use since 1970. Porcine aortic valves preserved by the "SGP" process are sutured to a Dacron cloth-covered flexible polypropylene stent. A radio-opaque Stellite metal ring encircles the stent and helps maintain orifice shape and proper leaflet coaptation. Model 242 is used for aortic valve replacement while model 342 is used in the mitral and tricuspid valve areas. These models differ only in the shape of their sewing rings.

The Hancock Modified Orifice aortic bioprosthesis (HMO-250) differs from the other two models by having replaced the right coronary leaflet, which contains a portion of septal endocardium with a non-coronary leaflet of an appropriate size. This valve modification was accomplished in an attempt to increase the effective flow orifice for use in patients with a small aortic annulus. The first clinical implant of a HMO-250 bioprosthesis was in October 1976.

IN VIVO PRESSURE DROPS: HANCOCK (STANDARD MODEL 242) AORTIC

Continued

Tissue Annulus Size mm	Rest N	MG mmHg	PG mmHg	CO ℓ-min^{-1}	VA cm^2	Exercise N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA$_2$ cm^2	ref#
25	16	10.1 (0-30)		4.9	NA						328
27	2	9	15 (10-20)	4.4	1.61 (1.5-1.65)	2	NA	21		NA	326
	3	18 (11-30)	17 (0-42)	NA	1.46 (0.9-2.1)						325
	6	4.0		5.5	NA						328
	1	19	8	NA	0.9						325

TABLE 48

IN VIVO PRESSURE DROPS: HANCOCK MITRAL VALVE (MODEL 342)

Tissue Annulus Size mm	Rest N	Rest MG mmHg	Rest PG mmHg	Rest CI ℓ-min^{-1}/m^2	Rest VA cm^2	Exercise N	Exercise MG mmHg	Exercise PG mmHg	Exercise CI ℓ-min^{-1}/m^2	Exercise VA cm^2	ref#
23	2	21.1±0.4**		NA	1.3						345
25	5	17.8+5.2**		NA	1.46±0.18**						345
27	8	13.1±3.2**		NA	1.89±0.41**						345
	1	12		2.4	NA						325
29	8	12.0±2.4**		NA	2.05±0.27**						345
	5	5 (4-8)		2.8 (2.3-3.3)	NA						325
	20	5.2 (0-10)		NA	2.1						323
31	8	10.3±3.4**		NA	2.15±.37**						345
	2	5		2.4	NA						325
	12	2.3 (0-8)		NA	2.9						323
33	9	8.7±2.2**		NA	2.47±0.35**						345
	4	5 (4-6)		2.9 (2.4-4.0)	NA						325
	10	2.5 (0-10)		NA	2.9						323

** ± SD

Sizes and Dimensions

Size	Sewing Ring Diameter(mm)	Valve Height (mm)		Internal Stent Diameter(mm)	Internal Stent Orifice Area(cm^2)
		models 242&250	model 342		
19	19	15	11	16.0	2.01
21	21	16	12	18.0	2.54
23	23	18	13	20.0	3.14
25	25	19	14	21.8	3.73
27	27	20	16	22.5	3.98
29	29	21	17	24.3	4.64
31	31	23	17	26.2	5.39
33	33	-	18	27.9	6.11
35	35	-	20	29.8	6.97

(b) In Vivo Results

Since the Hancock valve is the grandfather of the tissue valve bio-prostheses, there are many articles in the open literature on its long-term clinical performance. The standard model aortic valve has calculated VA's of 0.97 to 1.8 cm^2 for valve sizes of 19 to 27 mm (Table 46). In the mitral position calculated VA's ranged from 1.3 to 2.9 cm^2 for valves sizes of 23 to 35 mm (Table 48). The modified orifice aortic valve had VA's of 0.89 to 1.75 cm^2 for valve sizes of 19 to 25 mm (Table 47). Comparing the results in Tables 46 and 47, it is not immediately obvious that the modified orifice valves are less stenotic than the standard model valves. As stated by Rossiter, et al., (338) the hemodynamic differences between the two valve types are small, and the putative clinical advantages inherent in the use of the modified orifice valve remain to be completely defined. Both designs of Hancock valves are, however, more stenotic compared to the Ionescu-Shiley pericardial valve. Clinically significant hemolysis is not a major problem with

TABLE 50

IN VITRO PRESSURE DROPS: HANCOCK MITRAL VALVES

Tissue Annulus Diameter mm	Model #	$\bar{\Delta p}$ mmHg	CO ℓ/min	Q_{rms} ℓ/min	VA cm^2	RV cm^3/stroke	Ref #
19**	250(MO)	49.21		19.98	0.92	0.7(@100 min^{-1})	413
19**	242	74.04		19.98	0.75	0.8(@100 min^{-1})	413
19**	250(MO)	29.9		16.6	0.9		
21**	250(MO)	31.49		19.98	1.15	1.1(@100 min^{-1})	413
21**	242	46.15		19.98	0.95	1.0(@100 min^{-1})	413
23**	250(MO)	25.03		19.98	1.29	1.0(@100 min^{-1})	413
23**	242	31.49		19.98	1.15	1.4(@100 min^{-1})	413
25**	250(MO)	17.34		19.98	1.55	1.1(@100 min^{-1})	413
25	342	25.82		19.98	1.27	1.3(@100 min^{-1})	413
25**	250(MO)	10.7		16.6	1.64		200,168
27	342	18.02		19.98	1.52	1.3(@100 min^{-1})	413
29**	242	13.00		19.98	1.79	1.2(@100 min^{-1})	413
29	342	7.39		16.6	1.98		200,168
29	342	N/A		$\sim$100-300($\bar{Q}$)	$\sim$ 1.8		201
29	342	N/A	5-7.2	N/A	1.79		419 p 181
31	342	11.18		19.98	1.93	1.8(@100 min^{-1})	413
33	342	12.44		19.98	1.83	1.4(@100 min^{-1})	413
33	342	N/A	5-7.2	N/A	2.41		419 p 181

**studied in the mitral position

TABLE 51

HEMOLYSIS — HANCOCK PORCINE VALVE

Position	Model #	LDH	Hgb	Hapt	Other	Remarks	Ref#
M,T		204±52 IU/L (130-360)*	NA	94±52 mg% (50-250)*	plasma hgb .58±1.55 (0-6)*	2/22 had anemia 22/22 had mild hemolysis	337
double		NA	NA	NA		one pt had severe hemolytic anemia when the struts were bent inward	330
M		565 U/L	NA	NA		red cell damage by dacron-covered sewing ring & stents-one pt.	383
M		NA	NA	NA		no clinically significant hemolysis in 85 patients	333

*normal values

± SEM

TABLE 52

THROMBOEMBOLIC COMPLICATIONS : HANCOCK PORCINE VALVE

Position	Model#	Patient Ratio	Rate % per pt-yr	Deaths	Anticoagulation	Remarks	Ref #
A		1/65	NA	0	none		193
A,M,T		NA	NA	6(early) 3(late)	none	370pts studied;9/34 valves recovered had thrombosis on outflow side of valve; all 9 were mitral prostheses.	194
M		18/243	NA	NA	NA		195
M		1patient	NA	1	none	small thrombi on valve cusps	329
M,T		1/11	NA	NA	none		333
M		3/33	NA	1	warfarin for first 6 wks.	thrombus on 2 cusps and on ventricular aspect of mitral valve caused death	324
T		1patient	-	-	-	fibrin deposition on cusps	336
M		1patient	NA	1	none	large muscle shelf caused thrombus on sewing ring & atrial wall	332
A,M		26/211	NA	7	few on warfarin	6 early TEC 's (one month)	327
A,M		12/193	NA	NA	none		323
A,M		0/25	NA	NA	first 8 weeks		321
M		20/272	4.1	NA	first 3 months	2 thrombosed valves	319

THROMBOEMBOLIC COMPLICATIONS : HANCOCK PORCINE VALVE (continued)

Position	Model#	Patient Ratio	Rate % per pt-yr	Deaths	Anticoagulation	Remarks	Ref #
A,M,T		2/103	1.7	0	first 6-8 weeks		377
M		3/56	NA	0	none	all TEC's in patients with atrial fibrillation	373
A,M,T		0/91	NA	0	none		376
A		18/481	1.8	0	none		338
A	modified orifice	4/156	4.4	0	none		338
A		NA	1.7	1	first 6 weeks		335
M		NA	2.6	1	first 12 weeks		335
double		NA	1.6	1	first 12 weeks		335
A		2/124	NA	0	none		325
A		3/60	1.28	0	80% of pts had none; rest had anticoagulation for first 3-6 months		444
M		14/125	2.87	3	all patients with atrial fibrillation		444
double		2/36	1.37	0	all patients with atrial fibrillation		444

Flow visualization studies (141, 180, 199, 236) indicate that the flow that emerges from the Hancock valves, standard and modified orifice, is jet-like. Schramm, et al., (141) in their study showed that there was no reattachment of the jet. At a steady flow rate of 18l/min they observed a peak jet velocity of 180 cm/s with a size 25 modified orifice valve. Wright (180, 199) in his studies observed a vortex swirl in addition to the jet. High speed photography by Rainer et al., (209) showed that there was high frequency fluttering of the muscle-shelf leaflet during end-systole, with the aortic Hancock valve. No published velocity and shear stress measurements on the Hancock valve were encountered in our literature review. The primary reason for this being the company's past "policy" of not providing valves free of charge to engineering investigators. It is the only company which maintained such a "policy." It is our opinion, however, that the velocity and shear stress measurements downstream from the Hancock valves will be quite similar to those obtained with Carpentier-Edwards porcine valves. Gabbay et al., (200) state that there is no difference in pressure drop characteristics between the Carpentier-Edwards and modified orifice Hancock valves of corresponding sizes.

(d) Correlation

The in vivo and in vitro pressure gradient information clearly show that the Hancock porcine valves are stenotic especially in the smaller sizes. Patients with these valves wil not be able to lead very active lives due to large gradients across these valves under exercise conditions. The stenotic nature of the valve is in part due to the

10.

CARPENTIER-EDWARDS PORCINE VALVE

(a) Valve Description

The Carpentier-Edwards bioprosthesis is composed of porcine aortic valve leflets preserved in a buffered gluteraldehyde solution and mounted on a man-made flexible stent. The frame is made from a light weight corrosion resistant alloy called Elgiloy (cobalt-nickel alloy). The metal frame is covered with porous knitted Teflon cloth. Model 2625 is used for aortic valve replacement while model 6625 is used for mitral valve replacement. These models only differ in the shape of their sewing rings. The Carpentier valve has been in clinical use since 1975.

Sizes and Dimensions

Size	Sewing Ring Diameter(mm)	Valve Height (mm)	Stent Orifice Diameter(mm)	Support Orifice Area(cm^2)
21	21	16	18	2.40
23	23	17	20	3.24
25	25	18	22	4.19
27	27	20	23	4.34
29	29	21	25	5.11
31	31	22	27	5.93
33	33	22	29	6.80

TABLE 54

IN VIVO PRESSURE DROPS: CARPENTIER-EDWARDS MITRAL VALVE

Tissue Annulus Size mm	Rest N	MG mmHg	PG mmHg	CO ℓ-min^{-1}	VA cm^2	Exercise N	MG mmHg	PG mmHg	CO ℓ-min^{-1}	VA$_2$ cm	ref#
27	3	7 (7)		4.2 (3.6-5.0)	1.68 (1.44-1.82)	2	20 (19-21)		8.8 (8.4-9.1)	2.41 (2.06-2.77)	241
29	7	6.7 (3-10)		4.0 (3.2-6.5)	1.94 (1.54-3.67)	5	14 (9-32)		6.6 (4.2-11.3)	1.82 (1.48-2.67)	241
31	3	5 (4-6)		4.4 (3.7-4.8)	2.79 (2.23-3.81)	3	9.3 (6-14)		6.9 (5.2-9.1)	3.41 (2.89-4.83)	241
33	2	4.5 (3-6)		5.7 (3.8-7.5)	3.09 (2.28-3.9)	1	10		5.8	2.39	241

TABLE 55

IN VITRO PRESSURE DROPS: CARPENTIER-EDWARDS AORTIC VALVE

Tissue Annulus Diameter mm	Model #	$\bar{\Delta p}$ mmHg	CO ℓ/min	Q_{rms} ℓ/min	VA cm^2	RV cm^3/stroke	Ref #
21	2625	37.5	∿5.3	20	1.05	0.8(@70 min^{-1})	425
25	2625	18.0	∿5.3	20	1.52	1.2(@70 min^{-1})	425
27	2625	11.0	∿5.3	20	1.95	0.9(@70 min^{-1})	425

Average turbulent shear stresses during peak velocities were estimated to be on the order of 4200 dynes/cm^2. Yoganathan, et al., (349, 425) measured the velocity field downstream from a #27 aortic valve at steady flow rates of 10 and 25 l/min. The velocity profiles obtained were jet like, and also showed a region from flow separation and recirculation near the walls immediately downstream from the valve sewing ring. The effects of the jet were observed even 60 mm downstream from the valve. The turbulent shear stresses were on the order of 1000-3000 dynes/cm^2 and wall shears on the order of 200 to 600 dynes/cm^2. In addition, Yoganathan, et al., (349, 425) have photographed the opening and closing motion of the valve leaflets under pulsatile flow (sizes 27, 25 and 21). It was observed that the leaflets did not open symmetrically or reproducibly. The leaflets opened less at lower cardiac outputs (2.5 l/min) compared to normal cardiac outputs (5.0 l/min). It was also observed that the muscle-shelf leaflet was the last to open and the first to close. The valve leaflets only opened to about 50% of their approximate primary orifice areas. Gabbay, et al., (200) have made similar observations. High speed photography by Rainer, et al., (209) indicated that the leaflet with the muscle shelf exhibited high frequency vibrations during end systole.

(c) Correlation

The in vivo and in vitro pressure drop data indicate very clearly that this porcine valve design is also stenotic especially in the small sizes. Patients with these valves would find exercise strenuous and difficult. The in vitro valve photography showed that the leaflets do not open adequately, especially at low flows. This is therefore one of

TABLE 58

THROMBOEMBOLIC COMPLICATIONS : CARPENTIER - EDWARDS PROCINE VALVE

Position	Model#	Patient Ratio	Rate % per pt-yr	Deaths	Anticoagulation	Remarks	Ref #
A	2625	14/12,650	NA	NA	NA	10 had thrombosed valves	245
M	6625	15/12,838	NA	NA	NA	8 had thrombosed valves	245
A,M	NA	0/55	NA	0	first 3 months		386

11.

IONESCU-SHILEY PERICARDIAL VALVE

(a) Valve Description

The Ionescu-Shiley pericardial xenograft consists of three equal cusps which are mounted on a man made symmetrical titanium stent covered with Dacron cloth. The pericardial tissue which is obtained from the calf is treated and fixed in a buffered gluteraldehyde solution. The valves are then subsequently stored in 4% buffered formaldehyde to insure sterility. Although the pericardial valve was first used in clinical trials in 1971, it was first released for general use in the U.S.A. in 1976 as the Ionescu-Shiley prosthesis. The essential dimensions of the different size Ionescu-Shiley valves as obtained from Shiley laboratories, Inc., are given below. The valve has a universal sewing ring.

Size and Dimensions

Size	Sewing Ring Diameter (mm)	Valve Height (mm)	Orifice Diameter (mm)	Estimated Orifice Area(cm^2)
15	15	12	11.4	1.02
17	17	13	13.4	1.41
19	19	14	15.4	1.86
21	21	15	17.4	2.38
23	23	17	19.4	2.96
25	25	18	21.4	3.60
27	27	19	23.4	4.30
29	29	20	25.4	5.07
31	31	22	27.4	5.90
33	33	24	29.4	6.79

IN VIVO PRESSURE DROPS: IONESCU-SHILEY AORTIC VALVE
(continued)

Tissue Annulus Size	Rest					Exercise					ref#
	N	MG mmHg	PG mmHg	CO ℓ-min^{-1}	VA cm^2	N	MG mmHg	PG mmHg	CO ℓ-min^{-1}	VA cm^2	
23 & 25	4-23 2-25	NA	8.0±0.6*	3.1±0.2(CI)*	1.6±0.1*		NA	17.5±0.1*	4.4±3.2(CI)*	2.1±.1*	301
27	1	5	0	NA	2.1		6	1.0	NA	2.4	313
	2	3.3 (3.4-4.2)	NA	5.2(CO) (3.8-6.5)	2.7						299
31	1	1.7	NA	3.8(CO)	3.2						299

*± SEM

(b) In Vivo Results

In vivo VA's of 0.9 to 3.2 cm^2 were calculated for aortic valve sizes of 19 to 31 mm (Table 59). Mitral VA's varied from 1.2 to 2.4 cm^2 for valve sizes of 25 to 29, (Table 60). These results also indicate that the calculated VA's increase under exercise conditions (ie: increasing cardiac output). Thromboembolic events have been documented for this valve with TEC rates of 0.42 to 3.34% per pt. yr. (Table 64). No thrombosed valves have been documented. Articles published to date indicate that this valve could cause mild to moderate hemolysis even though the body can compensate for it. Since this valve has been in wide spread use only during the past four to five years the literature is incomplete. Dr. Harrison has observed excess fibrotic tissue on the sewing rings and up the outflow bases of the leaflets of recovered Ionescu-Shiley valves (439). A similar observation has been made by Dr. Trusler on a valve recovered from a 3 year old child (341). He also observed early calcification of the leaflets.

(c) In Vitro Results

Tables 65 and 66 indicate calculated VA's of 1.49 to 2.86 cm^2 for the size 21 through 31 valves. The calculated VA's for the Ionescu-Shiley valve in the mitral position obtained by Wright (413) are lower than those obtained by Gabbay and his co-worker (168, 200) and Walker, et al., (201). Results obtained in our laboratory (425) tend to agree better with those of Gabbay, et al., and Walker, et al. Regurgitation volumes are higher than for the porcine type valves. High speed photography has shown that the leaflets of the Ionescu-Shiley valves open uniformly and do not flutter (209). Photography studies in our laboratory indicate that the leaflets of the Ionescu Shiley valves

TABLE 62

IN VITRO PRESSURE DROPS: IONESCU-SHILEY MITRAL VALVE

Tissue Annulus Diameter mm	Model #	$\bar{\Delta p}$ mmHg	CO ℓ/min	Q_{rms} ℓ/min	VA cm^2	RV cm^3/stroke	Ref #
19	ISUD	18.25		16.6	1.26		168,200
21	ISUD	24.64		19.98	1.30	2.1(@100 min^{-1})	413
23	ISUD	17.11		19.98	1.56	3.4(@100 min^{-1})	413
25	ISUD	17.56		19.98	1.54	3.1(@100 min^{-1})	413
25	ISUD	7.7		16.6	1.93		168,200
27	ISUD	14.58		19.98	1.69	5.2(@100 min^{-1})	168,200
29	ISUD	9.27		19.98	2.12	4.8(@100 min^{-1})	413
29	ISUD	3.3		16.6	2.96		168,200
29	ISUD	≈ 1.5-6.0		≈ 100-300($\bar{Q}$)	≈ 2.5		201
31	ISUD	5.09		19.98	2.86	6.35(@100min^{-1})	413

TABLE 63

HEMOLYSIS — IONESCU-SHILEY PERICARDIAL VALVE

Position	Model #	LDH	Hgb	Hapt	Other	Remarks	Ref#
A		402 IU/L (range 294-580) (90-215)*	13.8 g% (range 12.5-16) (12.5-18)*	15 mg/dl (range 10-28) (170-300)*		10/10 had chronic hemolysis	218
M		306.2 IU/L (range 285-333) (90-200)*	13.7 g% (range 12.8-14.6) (12.5-18)*	26.5 mg/dl (range 12-53) (170-300)*		8/8 had mild to moderate hemolysis	300
M		normal	NA	normal		12 pts had no clinically significant hemolysis	18
A,M		NA	NA	NA		24 pts had no clinically significant hemolysis	301

* normal values

up the outflow faces of the leaflets. The region of flow separation observed adjacent to the valve leaflets could in addition lead to a build up of thrombotic, fibrotic and/or calcific materials on the outflow surfaces of the leaflets, as observed with the Hancock porcine valves. The wall shears could cause sublethal damage to endothelial tissue, while the turbulent shear stresses could lead to sublethal and/or lethal damage to blood elements. Such damage could lead to hemolysis, and thromboembolic problems as observed clinically.

TABLE 65

IN VIVO PRESSURE DROPS: ST. JUDE AORTIC VALVE

Tissue Annulus Size mm	Rest N	Rest MG mmHg	Rest PG mmHg	Rest CI ℓ-min^{-1}/m^2	Rest VA cm^2	Exercise N	Exercise MG mmHg	Exercise PG mmHg	Exercise CI ℓ-min^{-1}/m^2	Exercise VA cm^2	Ref#
19	6		13.8 (0-30)	3.2 (2.7-3.3)	1.5 (1.2-1.6)						131 p. 26
	3		11.0	3.1	1.38						130
21	2		9.0	4.95(CO)	1.15						130
	12	5.2±5.3**		3.9±0.9** (CO)	2.7 ±1.5**	12	12.1±6.9**		6.8±1.2** (CO)	2.2±1.0**	129
	15		6.0 (0-26)	2.7 (1.4-3.6)	2.1 (1.0-4.7)						131 p. 26
	4		1.0 (0-3.0)	3.25 (2.7-3.7)	NA	4		3.0 (0-6.0)	4.37 (4.1-4.7)	NA	131 p. 10
23	5		1.60	3.3	2.26						130
	11	3.2±3.8**		4.4±1.0** (CO)	3.6±1.7**	8	8.7±4.7**		7.0±2.1**	2.8±1.5**	129
	14		2.2 (0-6)	3.0 (2.0-4.0)	2.4 (1.25-3.47)						131 p. 26
	7		1.0 (0-4.0)	3.27 (2.9-3.5)	NA	7		2.6 (0-8.0)	4.6 (4.0-4.9)	NA	131 p. 10
25	14		2.07	3.21	2.26						130
	5	3.4±1.8**		4.0±0.8** (CO)	3.0±1.5**	3	4.9±4.6**		6.6±0.7** (CO)	4.6±3.2**	130
	30		2.6 (0-11)	3.0 (2.0-4.0)	2.7 (1.5-5.5)						131 p. 26
	11		2.0 (0.50)	3.36 (2.5-3.9)	NA	5		6.3 (0-24.0)	4.92 (3.3-6.0)	NA	131 p. 10

** ± SD

TABLE 66

IN VIVO PRESSURE DROPS: ST. JUDE MITRAL VALVE

Tissue Annulus Size mm	Rest					Exercise					
	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA$_2$ cm^2	ref #
23	1		4.4	4.4	2.1						131 p. 26
25	4		2.0 (0-4.0)	3.8 (3.1-4.5)	2.9 (2.5-3.09)						131 p. 26
	1		2.8	4.5	3.0						131 p. 54
	2	1.4±0.2**		3.3±0.6** (CO)	2.1±0.5**						129
27	20		1.2 (0-4.0)	3.3 (1.8-4.5)	3.1 (1.68-3.67)						131 p. 26
	10		1.24	3.6	3.30	10		1.48	4.0	3.4	131 p. 54
	5	1.9±0.6**		3.6±0.4** (CO)	2.1±0.4**	3	3.6±2.0**		6.4±0.9** (CO)	3.5±1.6**	129
29	33		1.2 (0-9.0)	2.7 (1-4.8)	3.1 (0.98-4.4)						131 p. 26
	5		0.55	3.8	4.0	5		0.70	4.2	4.1	131 p. 54
	16	1.8±0.8**		3.6±0.7** (CO)	2.8±1.0**	13	3.6±2.0**		6.4±0.9** (CO)	4.4±2.2**	129
	8	2.46+1.06**		2.5±0.6**	2.8±1.3**	8	7.0±3.2**		4.0±0.9**	3.2±1.3**	391
31	9		3.4 (0-8.0)	2.9 (1.4-4.3)	2.7 (1.0-5:2)						131 p. 26
	4		0.3	4.1	4.57	4		0.4	4.4	5.1	131 p. 54
	3	1.6±0.4**		4.6±0.8** (CO)	3.1±0.9**	3	3.2±1.3**		8.4±0.9** (CO)	4.3±1.5**	129

** ± SD

TABLE 67

IN VITRO PRESSURE DROPS: ST. JUDE AORTIC VALVE

Tissue Annulus Diameter mm	Model #	$\bar{\Delta p}$ mmHg	CO ℓ/min	Q_{rms} ℓ/min	VA cm^2	RV cm^3/stroke	Ref #
19			5-7.2		1.4		419 p 181
21			5-7.2		1.77		419 p 181
23			5-7.2		2.19		419 p 181
25			5-7.2		2.66		419 p 181
25		4.0	∿ 5.3	20	3.23		425
27		5.4	∿ 7.5	30	4.17		425
*27		∿3.8		20	3.31		177
27			4.0			13.3(@50 min^{-1})	237
27			5-7.2		3.16		419 p 181

*steady flow data

(c) In Vitro Results

In vitro flow studies indicate that this valve has the lowest pressure drops of any of the prostheses in current clinical use. A recent study by Dellsperger, et al., (237), however, indicate that this valve may have significant a regurgitant volume at low heart rates and low cardiac outputs.

Flow visualization studies in aortic and mitral chambers under both steady and pulsatile flow indicate smooth central type flow downstream from the valve (141, 137, 211, 236, 306). Initial velocity and shear stress measurements have been made by Yoganathan, et al., with size 27 and 25 aortic valves (372, 415 p. 295, 425). The measurements were made under steady flow rates of 10 and 25 1/min. The velocity measurements indicate that the flow field that emerges from the valve is centralized with low turbulence intensities. The measurements showed a region of flow separation immediately downstream from the sewing ring and adjacent to flow channel walls. Wall shear stresses on the order of 50 to 600 dynes/cm^2 were measured together with estimated turbulent shear stresses of 100-600 dynes/cm^2. Velocity measurements have not been made close to the pivoting mechanism of the valve. Schramm, et al., under steady flow conditions have also observed flow separation occurring from the downstream sewing ring (141). They state that the flow separation generates a circular dead water region which surrounds the main flow. Studies in our laboratory (425) and by Rainer, et al., (451) indicate asynchronous closing of the two leaflets in pulsatile flow. We have also observed that particles of dirt in the blood analog fluid cause sticking of the valve leaflets.

TABLE 70

THROMBOEMBOLIC COMPLICATIONS : ST. JUDE BI-LEAFLET VALVE

Position	Model#	Patient Ratio	Rate % per pt-yr	Deaths	Anticoagulation	Remarks	Ref #
A,M		1/88	NA	0	79/88 on warfarin		129
M		0/23	-	0	coumadin		125
A		0/25	-	0	coumadin		125
A,M		8/65	NA	1	none; on platelet inhibiting agents only	4 valves had dysfunction due to thrombosis	132 p 7
A,M		6/115	NA	2	NA		132 p 31
A		0/71	-	0	acenocoumarol or aspirin and dipyridmole		132 p 45
M		1/50	NA	NA			132 p 45
double		1/29	NA	NA			132 p 45
M		12/1341	1.2	NA	majority on coumadin	4 thrombosed valves	132 p 59
A		12/1873	.9	NA	majority on coumadin		132 p 59
A		0/24	-	0	NA		132 p 72
M		0/15	-	0	NA		132 p 72
M		2/82	NA	NA	all patients		132 p 25
A,M		0/24	-	0	coumadin		132 p 6
A		0/71	-	0	acenocoumarol		131 p 24
M		1/50	.23	NA	acenocoumarol		131 p 24
A,M		0/87	-	0	coumadin	2 yr follow up	132p.6

(d) Correlation

The in vivo and in vitro results indicate clearly the superior pressure drop characteristics of the St. Jude prosthesis. This is a tremendous advantage for patients who lead active lives, as well as for children and adults with small valve annuli (129, 130; 131 p. 10, 26 & 54; 419 p. 181). The regurgitation volumes observed in vitro at low heart rates could be significant at low cardiac outputs. One of the reasons for this result could be the asynchronous closing of the leaflets. The asynchronous closing of the leaflets is in our opinion an inherent problem with any bileaflet design, since you can not make both leaflets identical. The central flow field created by the valve is an advantage. The wall shears could cause sub-lethal damage to the endothelial lining of the vessel walls especially in the aortic position, while the turbulent shear stresses could cause sub-lethal and/or lethal damage to blood elements. It is therefore not surprising to observe mild hemolysis and TEC events, with this prosthesis. The region of flow separation could cause excess tissue growth on the downstream sewing ring which in turn could lead to valve dysfunction by impeding movement of the leaflets. This situation could be aggravated by certain surgical techniques such as using pledgets to sew the valve into place. It is therefore of utmost importance that the physician be able to monitor the movement of the leaflets under cinefluoroscopy. One of the major clinical disadvantages of the St. Jude valve is its poor radiographic visibility, especially if the physician is not familiar with the prosthesis. The problem of leaflets sticking has not been documented in the medical literature, but our observations in the pulse

13.

HALL-KASTER TILTING DISC VALVE

(a) Valve Description

The Hall-Kaster valve is composed of a tilting disc of pyrolytic carbon within a titanium housing. The housing is machined from a single piece of solid titanium, eliminating the need for welds. The disc pivots to an angle of 75 degrees in the aortic model, and 70 degrees in the mitral model, in the fully open position. The disc is marked by a radio-opaque marker. The sewing ring is made of knitted Teflon. The valve has been in clinical trials since 1978 and was recently approved for general clinical use by the FDA.

Sizes and Dimensions

Size	Sewing Ring Diameter(mm)	Orifice Diameter (mm)	Primary Orifice Area(cm^2)
21	21	16	2.01
23	23	18	2.54
25	25	20	3.14
27	27	22	3.80
29	29	24	4.52
31	31	24	4.52

(b) In Vivo Results

The Hall-Kaster tilting disc prosthesis has like the St. Jude valve been in clinical evaluations since 1978. It was recently approved by the FDA for general clinical use (December 1981). Approximately five thousand of these devices have been implanted world wide and a majority of them in Europe. In vivo clinical data indicate good

TABLE 72

IN VIVO PRESSURE DROPS: HALL-KASTER MITRAL VALVE

Tissue Annulus Size mm	Rest N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA cm^2	Exercise N	MG mmHg	PG mmHg	CI ℓ-min^{-1}/m^2	VA$_2$ cm^2	ref#
27	3		6.0±4.4**	NA	3.03±0.58**						400
	3		6.0	4.9 (4.1-5.6)	3.08						402
29	3		4.7	NA	3.18	3		11.0		NA	402
	2		NA	NA	2.86±1.46**						400
	8		2.1	NA	3.44	8		4.7	NA	NA	402
	7		2.0±0.7**	NA	3.35±0.77**						400

** ± SD

TABLE 73

IN VITRO PRESSURE DROPS: HALL-KASTER AORTIC VALVE

Tissue Annulus Diameter mm	Model #	$\bar{\Delta p}$ mmHg	CO ℓ/min	Q_{rms} ℓ/min	VA cm^2	RV cm^3/stroke	Ref #
21	AHK	13.5	∿ 5.3	20	1.76	5.4	425
25	AHK	5.25	∿ 5.3	20	2.82	7.8	425
27	AHK	6.5	∿ 7.5	30	3.80	9.0	425

500 dynes/cm^2 and maximum turbulent shear stresses (estimated from turbulence intensity measurements) to be on the order of 500 to 1500 dynes/cm^2. A region of flow separation was observed in the minor outflow region adjacent to the sewing ring and flow channel walls. In addition, small regions of stagnation existed immediately downstream from the two metal pivot stops in the major orifice, and along the pivot post of the minor orifice.

(d) Correlation

In vivo and *in vitro* pressure measurements indicate that the Hall-Kaster valve has improved pressure drop characteristic compared to the Lillehei-Kaster and Bjork-Shiley tilting disc valves. At low heart rates and low cardiac outputs (for example, immediately after open heart surgery) the regurgitant volume across this valve design could be significant.

The wall shears created by the valve could cause sublethal damage to the endothelial lining of vessel walls especially in the aortic position. The measured *in vitro* turbulent shear stresses could lead to sublethal and/or lethal damage to red cells and platelets. Therefore it is not surprising that mild to moderate hemolysis and thromboembolic problems are clinically observed with this prosthesis. Other possible reasons for the hgh LDH levels measured in patients (indication of hemolysis) with this valve design are: (a) the large amount of exposed metal on the prosthesis superstructure, and (b) leakage through the central pivot hole when the valve is closed. If most of the leakage volume occurs through this central pivot hole, the shear stresses

TABLE 76

THROMBOEMBOLIC COMPLICATIONS : HALL-KASTER TILTING DISC VALVE

Position	Model#	Patient Ratio	Rate % per pt-yr	Deaths	Anticoagulation	Remarks	Ref #
A	AHK	7/233	2.3	1	all patients		400
A	AHK	1/113	NA	0	all patients		401
M	MHK	0/22	0	0	all patients		402
M	MHK	8/112	7.8	2	all patients		400
double	AHK & MHK	2/57	3.4	0	all patients		400

III. CONCLUSIONS

Following the collection, analysis, and interpretation of the *in vivo* and *in vitro* information and data pertaining to the current state of the art in respect to the safety and performance of prosthetic heart valves (mechanical and tissue), Georgia Tech concludes that:

(1) At present we do *not* have an ideal prosthetic heart valve. During the past 20 years manufacturers have developed and produced various designs of prosthetic heart valves, some of which perform satisfactorily when implanted surgically in patients suffering from valvular heart disease. Other designs have had to be removed from the open marked due to lack of *adequate* safety and efficacy.

(2) There is a lack *in vivo* clinical and *in vitro* fluid dynamic data and information on all designs of prosthetic heart valves in current clinical use. The lack of good quality clinical information and data on some of the older valve types is surprising.

(3) Good long term clinical follow up data exists only for the following valve types studied: (i) Starr-Edwards ball valves, (ii) Bjork-Shiley tilting disc valve, (iii) Lillehei-Kaster tilting disc valve, and (iv) Hancock porcine valve.

(4) There is a lack of good detailed pathologic studies performed on heart valve prostheses recovered at surgery and/or autopsy. The lack of such studies will hinder the progress and development of not only better heart valve prostheses, but also other future artificial devices such as left ventricular assist devices and the total artificial heart.

(9) All prosthetic valves (mechanical and tissue) in current clinical use cause sublethal and/or lethal damage to blood elements such as red cells and platelets. The shear fields created by the valves are all capable of causing such damage. Sublethal damage to red cells could in time lead to mild hemolysis. Similarly, sublethal damage to platelets could over a period of time lead to thromboemboli and thromboembolic complications.

(10) All peripheral flow type valves cause damage to the endothelial lining of the proximal ascending aorta. This is directly related to the elevated wall shear stresses in the immediate downstream vicinity of these valves. They may also cause sublethal and/or lethal damage to the ventricular wall. Other mechanical designs and tissue bioprostheses could cause sublethal and/or lethal damage to the endothelial lining of the aortic wall. The jet type flow from the tissue valves could cause damage to the ventricular wall. Depending on the orientation of the valve the flow in the major orifice region of the tilting disc valve could also cause damage to the ventricular wall. Depending on the orientation of the valve the flow in the major orifice region of the tilting disc valve could also cause damage to the ventricular wall.

(11) All prosthetic valves in current clinical use cause hemolysis and thromboembolic complications, and are prone to the problems of thrombus formation and excess tissue growth on the valve superstructure.

(12) In many cases the hemolysis caused by the prosthesis is mild or moderate, and is generally compensated for quite adequately by the bone-marrow. Cloth covering on the valve superstructure (such as with

IV. RECOMMENDATIONS

1. Set up a national registry for prosthetic heart valves immediately. Detailed pathologic, and non-destructive and destructive engineering studies should be conducted on recovered valves, under the auspicies of the registry. At the time of valve implantation surgery, patients should be requested to sign a release so that the valve or valves may be recovered for scientific purposes at death. Current implant retrieval programs conducted by some of the manufacturers do not facilitate free transfer of information between medical and scientific communities. It seems as if those valve prostheses disappear from the public domain.

2. An educational program should be estimated for patients which provides reliable and accurate scientific information regarding the current status of various heart valve prostheses, their uses and limitations, and potential problems.

3. Require good clinical follow up data on all designs of valve prostheses. Such clinical follow up should include more detailed and sensitive tests to study blood component damage. For example, half-life studies should be conducted on tagged red cells and platelets. The filter ability of the red cells in micropores should also be studied. It may be necessary in the initial stages to sponsor such studies at a few major medical centers.

4. Standardized methodology should be established for reporting hemodynamic, hemolysis and TEC data. Such an effort would require the cooperation of the American Heart Association, American College of

community should appreciate the value of *in vitro* testing and the problems associated with such testing studies. On the other hand, the engineer should understand the problems faced by the cardiovascular surgeon and cardiologist. The collaboration and communication should take place in both directions.

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VI. NOMENCLATURE

A	aortic valve
CO	cardiac output (l/min)
CI	cardiac index ($l\ min^{-1}/m^2$)
Hapt	haptaglobin count
Hgb	hemoglobin count
LDH	lactodehydrogonase
M	mitral valve
MG	mean systolic or diastolic pressure drop (mm Hg)
mo	months
N	number of patients
NA	not available
PG	peak systolic or diastolic pressure drop (mm Hg)
$\overline{\Delta p}$	mean systolic or diastolic pressure drop (mm Hg)
pt	patient
pt.yr.	patient years
Q_{rms}	root mean square flow rate during systole or diastole (l/min)
$\overline{Q}$	mean flow rate during systole or diastole (l/min)
SD	standard deviation
SEM	standard error of the mean
RV	regurgitant volume (i.e.: closure plus leakage volumes) (cm^3/stroke)
T	tricuspid valve
TEC	thromboembolic complication
VA	calculated valve area (i.e.: EOA ≡ effective orifice area) (cm^2)

FINAL REPORT
Phase II

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

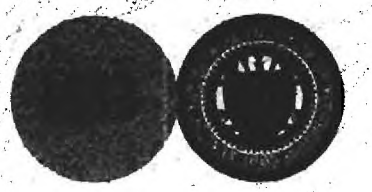
By
A. P. Yoganathan, Ph.D., Principal Investigator

Under
Contract No. 223-81-5000
Georgia Tech Research Institute (GTRI)
and
Bureau of Medical Devices (BMD)
Food and Drug Administration (FDA)
Wm. Letzing, Ph.D., FDA Project Officer

Duration of Study: 10/1/81 – 11/30/83

November 1983

GEORGIA INSTITUTE OF TECHNOLOGY
A UNIT OF THE UNIVERSITY SYSTEM OF GEORGIA
SCHOOL OF CHEMICAL ENGINEERING
ATLANTA, GEORGIA 30332



PHASE II FINAL REPORT (PART I)

PROSTHETIC HEART VALVES: A STUDY OF IN VITRO PERFORMANCE

NOVEMBER 30, 1983

Contract No. 223-81-5000

between

Georgia Tech Research Institute (GTRI)

and

Bureau of Medical Devices (BMD),

Food and Drug Administration (FDA)

Principal Investigator: A. P. Yoganathan, Ph.D.

FDA Project Officer: Wm. Letzing, Ph.D.

Duration of Study: 10/1/81 - 11/30/83

SUMMARY

The following report is a detailed experimental study of the *in vitro* fluid dynamic characteristics of different designs of prosthetic heart valves in current clinical use. The study was conducted under Food and Drug Administration contract # 223-81-5000, which lasted approximately two years. It should, however, be noted that due to the limitations of time and money not all the questions regarding the fluid dynamic performance of a given valve design could be answered. Since it is anticipated that the report will be read by scientists, engineers and physicians, the report has been written in three parts.

Part I summarizes the *in vitro* fluid dynamic characteristics of each valve design (ie: the experimental results), and attempts to relate these results to possible clinical and pathologic problems. No comparisons are, however, made between the different valve designs. Part II contains the details of the experimental equipment and techniques used during the study. Part III contains the detailed experimental data in graphical, tabular and/or photographic forms. All the chapters, pages, figures, and tables are consecutively numbered in numerical order.

For the reader who is only interested in the overall results of the study, reading Part I of the report would be sufficient. Parts I and III of the report will be on microfilm with NTIS.

LIST OF PERSONS MAKING INPUT TO THIS STUDY

Principal Investigator:	Professor Ajit P. Yoganathan, Ph.D.
Collaborating Scientists:	Yi-Ren Woo, MS Frank P. Williams, MS Patrick D. Faughnan, MS Dana M. Stevenson, MS
FDA Officers:	William Letzing, Ph.D. Edward Mueller, Ph.D. Stephen Hilbert, Ph.D.

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CHAPTER I

INTRODUCTION AND BACKGROUND

The major objective of this project was to investigate the *in vitro* fluid dynamic characteristics of different designs of prosthetic heart valves, in both aortic and mitral flow chambers. The valves that were studied are listed below in Table 1, together with their sewing ring and primary orifice diameters.

In some instances the experimental methodology and techniques were changed from the original contract, based upon the findings of preliminary experiments. The philosophy that governed these changes was aimed at providing the FDA with the best possible scientific and engineering information, within the budget and time constraints of the project. Changes made during the contract are noted in the appropriate places within the text.

TABLE 1: PROSTHETIC HEART VALVES USED IN STUDY

Name of Valve	Sewing Ring Diameter mm	Internal Stent or Primary Orifice Diameter mm
Starr-Edwards 1260	27	17.0
Starr-Edwards 6120	28	18.0
Smeloff	26	17.1
Beall	28	16.5
Björk-Shiley (C-C)	27	22.0
*Medtronic-Hall (AHK)	27	22.0
*Medtronic-Hall (MHK)	27	22.0
St. Jude	27	22.3
Hancock (Std)	27	22.5
Hancock (MO)	25	21.8
Carpentier-Edwards	27	23.0
Ionescu-Shiley	27	23.4

*Formerly known as the Hall-Kaster valve

Heart valve prostheses have been used successfully since 1960. As stated by Roberts (1) the decade of 1960 will probably be remembered most in the annals of cardiology as the decade during which cardiac valve replacement became a successful reality. Of the nearly 50 different cardiac valves introduced over the past 20 years, many have been discarded due to their lack of success, and of those remaining, several modifications have been made or are being made at the time of this writing. The most commonly used basic types of prosthetic valves at present are (a) caged ball, (b) tilting disc, (c) caged disc, (d) bi-leaflet and (e) bioprosthesis. At present over 75,000 prosthetic valves of different designs are used annually throughout the world. Even after 20 years of experience the problems associated with heart valve prostheses have not been totally eliminated. The most serious problems and complications associated with heart valve prostheses are: (a) thromboembolism, (b) tissue overgrowth, (c) infection, (d) tearing of sewing sutures, (e) red cell destruction (hemolysis), (f) valve failure due to material fatigue or chemical change, (g) damage to the endothelial tissue lining of the vessel wall adjacent to the valve and (h) leaks caused by failure of the valve to close properly. Problems (a), (b), (e) and (g) are directly related to the fluid dynamics associated with the various prosthetic heart valves, and need to be addressed in more detail by investigators studying bio-fluid mechanics. The other problems are indirectly related to the fluid mechanics. The problems relating valve failure due to material fatigue or chemical change also need to be studied especially as they relate to bioprostheses.

Tissue bioprostheses gained wide spread use during the mid-1970's. It was even naively thought by some of the tissue valve manufacturers that the ideal heart valve prosthesis had been discovered. The major advantage of tissue bioprostheses compared to their mechanical counterparts is that they appear to have a lower incidence of thromboembolic complications. Therefore, tissue valves for a large part can be used without anticoagulation therapy to eliminate or reduce thromboembolic complications. Unfortunately, the tissue bioprostheses clinically used at present also have major disadvantages such as: (a) relatively large pressure drops compared to some of the mechanical valves, especially in the smaller sizes, (b) jet-like flow through the valve leaflets, (c) calcification, material fatigue and/or wear of valve leaflets, especially in children. Because of these and other drawbacks valve manufacturers are now developing new designs of mechanical valves such as the St. Jude, Medtronic-Hall and Omni-Science prostheses, newer designs of bioprostheses and trileaflet valves made from polymeric materials.

The ideal heart valve prosthesis has not yet been designed and probably will neven exist. An ideal valve should have the following characteristics:

1. Be fully sterile at the time of implantation and be nontoxic.
2. Be surgically convenient to insert at or near the normal location in the heart.
3. Conform to the heart structure rather than the heart structure conform to the valve (i.e., the size and shape of the prosthesis should not interfere with cardiac function).

4. Show a minimum resistance to flow so as to prevent a significant pressure drop across the valve.
5. Have minimal reverse flow necessary for valve closure, so as to keep the incompetence of the valve at a low level.
6. Show low mechanical and structural wear of the valve.
7. Be long-lasting (~25 years), and maintain its normal functional performance (i.e. must not deteriorate with time).
8. Cause minimum trauma to blood elements and the endothelial tissue of the cardiovascular structure surrounding the valve.
9. Show a low probability for thromboembolic complications without the use of anticoagulants.
10. Should not be noisy and disturb the patient.
11. Should be radiographically visible.
12. Should have a modest price.

As stated previously the serious problems of thromboembolism, excess tissue overgrowth, red-cell and platelet damage, and damage to the endothelial lining of the vessel wall adjacent to the valve are directly related to the fluid dynamics associated with the various types of valve prostheses. Blackshear and his co-workers (2,3) suggest that the shear stresses required in the bulk of the flow to hemolyze red blood cells are about 40,000 dynes/cm^2. Nevaril and his co-workers (4) contend, however, that this value could be as low as 1500 dynes/cm^2. In vitro experiments (5-7) have also recently shown that platelets could be damaged by shear stresses of the order of 100-500 dynes/cm^2. A formed element such as a red blood cell which adheres to the vessel wall or to a foreign surface (such as the valve superstructure) may be damaged by

shear stresses of the order of $10\text{-}10^2$ dynes/cm^2 (2, 3, 8). Lloyd, et al., (9) indicate that sublethal damage to red blood cells could occur at shear stresses on the order of 500 dynes/cm^2 or less. A recent study by McIntyre indicates that the red blood cells of heart valve patients are more filterable in micropores than compared to normal subjects, due to sublethal damage to the red cells of valve recipients. Lethal damage to red blood cells causes hemolysis which in turn leads to anemia. Sublethal and/or lethal damage to red blood cells could also lead to platelet adhesion, aggregation and coagulation, resulting in thrombus formation. Mechanical damage to platelets (lethal and sublethal) will eventually lead to thromboembolic complications.

Fry (10, 11) has conducted two studies on the effects of wall shear on the endonthelial lining of the aortic wall. He found that the endothelial cells on the vessel wall could be damaged at wall-shear stresses of about 400 dynes/cm^2 and could be eroded off the vessel wall at shear stresses of about 950 dynes/cm^2. He observed that when the endothelial surface was exposed to shearing stresses above some critical value (400 dynes/cm^2) the cells began to suffer structural and chemical changes. The critical stress is known as the "yielding" stress. If a shearing stress above the critical value is applied for a long time period, the yielding process continues until the cells become mechanically unstable and are washed away from their moorings to the basement membrane in total or by progressive erosion of cell substance. As the eroded surface of the vessel wall is exposed to the flowing blood, deposition of blood elements and thrombotic materials occur. Fry found that the deposited material consisted of fibrous tissue, platelets, red blood cells, and other unidentified debris. He states that such deposition could lead

to intimal thickening of the vessel wall. Woolf and Carstairs (12) state that the fibrous tissue observed on the aortic wall as a result of intimal thickening owes its pressence to either infiltration or thrombus formation, or a combination of these two factors.

Platelets do not adhere to intact endothelial cells but they do adhere to subendothelial connective tissue composed of collagen and other materials. Platelets, however, have access to collagen fibers once the endothelial lining of a vessel wall is damaged or eroded off. The adhesion of platelets to the damaged vessel leads to the subsequent release of ADP and platelet factor 3 (PF-3). These substances play an active role in platelet aggregation and coagulation, respectively, and may lead to thrombus formation. A red blood cell will not stick to the intact endothelial lining of a vessel wall. If, however, the vessel intima is damaged resulting in a loss of endothelial integrity, red blood cells could adhere onto the vessel wall. If the adhered red blood cell is exposed to shears on the order of 10 to 100 dynes/cm^2 it will probably be lethally damaged and hemolyzed. Red blood cells contain ADP and a clot-promoting factor known as erythrocin. These substances are released into the plasma as a result of rbc hemolysis initiating both platelet aggregation and coagulation, which in turn may lead to thrombus formation.

The mechanical damage to the blood elements, as well as to the endothelial tissue of the adjacent vessel wall, may in addition trigger the compelx biochemical reactions which could lead to the excess fibrous tissue overgrowth observed on some recovered heart valves. Therefore, large wall and bulk turbulent shear stresses could cause serious problems and complications in vivo.

It is also well known that regions of flow stagnation, flow separation and excessively low shear in the immediate vicinity of the valve superstructure have been related to thrombus formation and/or excess tissue overgrowth on the prosthesis. The flow velocity, shear stress and pressure fields in the immediate vicinity of a given heart valve prosthesis design are directly related to the fluid dynamic characteristics of the prosthesis. Therefore, detailed in vitro fluid dynamic studies should help predict potential problems and complications that may arise in vivo, with different designs of prosthetic heart valves.

CHAPTER 2

SUMMARY OF IMPORTANT RESULTS

I. VALVES IN THE AORTIC POSITION

(i) Starr-Edwards Model 1260 Ball Valve

The Starr-Edwards ball has poor pressure drop characteristics as indicated by a performance index (PI) of 0.30. The valve will be very stenotic under excercise conditions. The closure back flow (@ 70 beats/min) was 5.5 cm^3 /beat, while the leakage back flow was negiligible.

The forward flow emerging form this valve forms an axisymmetric circumferential jet. The velocity of the jet reaches a value of 180 cm/s at peak systole. The turbulent shear stress could be as large as 3000 dynes/cm^2 in the annular region between the ball and the flow channel wall. Such high shear stresses could cause sub-lethal and/or lethal damge to blood elements.

The circumferential jet separates from the surface of the ball at a 45 degree angle to the axial direction and impinges on the wall of the flow channel. The highest estimated wall shear stress is 1940 dynes/cm^2 , which is large enough to damage the endothelial lining of the aorta. A large wake exists distal to the ball and extends

about 50 mm downstream from the valve sewing ring. The region immediately downstream of the cage apex is relatively stagnant and is a probable site for thrombus formation.

An annular region of flow separation can be observed adjacent to the valve sewing ring, up stream of the circumferential jet. The low flow in this region makes the downstream sewing ring region, especially at the struts, vulnerable to thrombus formation and/or excess tissue growth. The measurements upstream of the valve during diastole show that the leakage back flow for this valve design is negligible.

(ii) Bjork-Shiley Convexo-Concave Tilting Disc Valve

The Bjork-Shiley valve had a PI of 0.45, which indicates that it could be stenotic under moderate to severe excercise conditions. The closing and leakage back flows were measured to be 4.5 cm^3 /beat and 4.0 cm^3 /beat , respectively. At low cardiac outputs (<3 l/min) the regurgitant volumes measured with this valve could become clinically significant.

The valve produces an uneven flow field, with the forward flow primarily going through the major orifice. The flow emerging form the major orifice is jet-like throughout the major portion of systole. The jet impinges

on the flow channel wall with high velocity and generates a wall shear stress of 1380 dynes/cm^2 . This high wall shear atress could cause damage to the endothelial lining of the aortic wall. A small region of flow separation exists adjacent to the major orifice sewing ring, between the major orifice jet and the flow channel wall. The velocity of the major orifice jet is about 210 cm/s at peak systole, with turbulent shear stresses on the order of 1800 dynes/cm^2 The flow region underneath the disc appears to be relatively stagnant throughout the systole. This region never gets "washed", which could lead to thrombus formation on the aortic face of the disc.

The flow field in the minor orifice region is much more disturbed than that in the major orifice region. The peak velocity of the minor orifice jet is about 210 cm/s. A large region of flow separation exists between the minor orifice jet and the flow channel wall. The low flow velocities adjacent to the sewing ring in the minor orifice region, could lead to tissue overgrowth along the sewing ring in this region. The obstruction of the valve occluder generates a shear stress as high as 3300 dynes/cm^2 just underneath the occluder. This high shear stress could cause sublethal and/or lethal damage to blood cells. Leakage back flow occurs adjacent to the flow channel wall, directly upstream of the annular gap between the occluder and the valve orifice ring, with a negative

velocity as high as -22 cm/s, and turbulent shear stresses on the order of 430 dynes/cm^2 .

(iii) Medtronic-Hall Tilting Disc Valve

The Medtronic-Hall tilting disc valve has good pressure drop characteristics (PI = 0.64). The regurgitation characteristics of this valve design could become clinically significant at low cardiac outputs (closure back flow 5.1 cm^3 /beat ; leakage back flow 4.3 cm^3 /beat).

The flow field produced by this valve design is also asymmertric, with the forward flow primarily occuring through the major orifice. High velocity jet-like flow can be seen from either orifice at peak systole. The highest velocities of these two jets are about the same magnitude (210 cm/s). High shear stresses are more spread out in the minor orifice than in the major orifice, which indicates that the flow in the minor orifice region is far more disturbed. A large region of flow separation exists in the minor orifice region adjacent to the sewing ring. The comparatively low fluid velocities in this region makes the downstream sewing ring in the minor orifice a vulnerable site for tissue overgrowth and/or thrombus formation. The metal strut superstructure in the major orifice appears to have only a small effect on the shear

stress field in the major orifice. In the minor orifice, a wake exists downstream of the strut and reduces the velocity sharply, which makes this strut structure a possible location for thombus formation. The highest shear stress observed over the entire systolic period occurred at the edge of the major and the minor orifice jets and was on the order of 2000 dynes/cm^2 . Such high shear stresses could lead to blood cell damage, especially in the minor orifice region where the shear stresses are elevated over the entire systolic period. The highest estimated wall shear stress was 700 dynes/cm^2 , and was measured at the location where the major orifice jet impinged on the flow channel wall. This high wall shear stress could cause sublethal damage to the endothelial lining of the aortic wall.

Back flow during diastole occurred as a very narrow intense jet through the central pivot hole , with a velocity of -30 cm/s and shear stresses as high as 680 dynes/cm^2 . Such shear stresses could cause blood cell damage.

(iv) St. Jude Bileaflet Valve

The St. Jude valve has the best pressure drop characteristics, PI = 0.71, of all the designs of prosthetic heart valves in current clinical use. The

regurgitation characteristics of this valve could create clinical problems at low cardiac outputs. The valve has a closure back flow of 5.5 cm^3 /beat , and a leakage back flow of 5.1 cm^3 /beat .

Flow through this valve forms three jet-like flow fields, two from the two side orifices and one from the center orifice. The flow emerging from the center orifice is more disturbed then that emerging from the side orifices. The jets from the side orifices are wider than that from the center orifice. This suggests that the major part of the volumetric flow tends to go through the side orifices. Regions of flow separation can be observed adjacent to the downstream sewing ring. The largest regions of flow separation occurs at either end of the center orifice (ie: near the pivot points), and would be the most likely locations for tissue overgrowth and/or thrombus formation to occur. Since the hinges of the valve leaflets are in these regions and leaflet motion is susceptible to easy interference, prosthetic valve dysfunction could occur.

The two leaflets of the St. Jude valve do obstruct the flow and reduce the fluid velocity distal to the leaflets, and also create high turbulent shear stresses. The highest turbulent shear stress measured was on the order of 2000 dynes/cm^2 . The measurement was made in the side orifice close to the valve leaflet at peak systole.

The highest turbulent shear stresses during the accelaration and decelaration phases are 1630 dynes/cm^2 and 1370 dynes/cm^2 ,respectively. These high shear stresses could lead to sublethal and/or lethal blood cell damage. Wall shear atresses with this valve design are generally low (~630 dynes/cm^2), but still can cause sublethal damage to the endothelial lining of the aortic wall. Leakage back flow occurs upstream of the central pivot of the valve during diastole, with a velocity as high as -16 cm/s and turbulent shear stresses on the order of 325 dynes/cm^2 .

(v) Carpentier-Edwards Bioprosthesis

This valve is without a doubt stenotic (PI = 0.34), and will be very stenotic under excercise conditions. The valve has a very small closing back flow (0.9 cm^3 /beat) and no measureable leakage during diastole. The leaflet motion characteristics of the Carpentier valve leave much to be desired. The valve leaflets only opened to 70% of the stent orifice area at a cardiac output of 7.5 l/min.

This valve produces a very high velocity jet-like flow, which emerges from the triangular opening of the valve leaflets. The jet does not dissipate until 65 mm downstream from the valve sewing ring. The velocity of the jet at peak systole is as high as 360 cm/s. Very high

turbulent shear stress exists in the narrow region around the edge of the jet, with values as high as 4400 dynes/cm^2 . Although this high shear stress only occurs at peak flow, sublethal and/or lethal damage to blood elements is very likely to occur.

The flow separates from the downstream edge of the leaflets. Regions of flow separation exist around the jet and extend as far downstream as 75 mm from the sewing ring, during decelaration phase. The annular region between the outflow surfaces of the leaflets and the flow channel wall is stagnant, which could lead to the deposition of thrombotic, fibrotic and/or calcific material on the outflow surfaces of the leaflets. The region of flow separation adjacent to the downstream sewing ring could lead to the build up of excess fibrotic tissue. The highest estimated wall shear stress with this valve was 460 dynes/cm^2 , which could cause sublethal damage to the endothelial lining of the vessel wall adjacent to the valve. There was no measurable leakage for this valve design.

(vi) Hancock Modified Orifice Procine Xenograft

Of the three procine valves studied in this project the Hancock modified orifice valve was the least stenotic (PI = 0.39). However, the pressure drop characteristics

indicate that the valve will become stenotic under moderate excercise conditions. The closing back flow for this valve was 0.8 cm^3 /beat . The valve leaflets opened to 80% of the stent orifice area (@ cardiac output of 7.5 l/min).

The valve produces a high velocity central jet which does not dissipate until 80 mm downstream from the valve sewing ring. The highest velocity measured was 330 cm/s. The high turbulent shear stresses (3000 dynes/cm^2) produced by this valve in the jet could lead to sublethal and/or lethal blood cell damage. However, this high turbulent region is confined to a narrow region around the jet. Flow separates from the downstream edge of the valve leaflets. A region of flow separation exists around the jet and extends 65 mm downstream of the sewing ring at peak systole. The annular region between the outflow surfaces of the leaflets and the flow channel wall is relatively stagnant. This region could lead to the deposition of thrombotic,fibrotic and/or calcific material on the outflow surfaces of the leaflets. The region of flow separation adjacent to the downstream sewing ring could lead to the build up of excess fibrotic tissue. The highest estimated wall shear stress was 490 dynes/cm^2 , which could cause sublethal damage to the endothelial lining of the aortic wall. The leakage back flow for this valve design is also negligible.

(vii) Ionescu-Shiley Pericardial Xenograft

The Ionescu-Shiley valve had pressure drop characteristics similar to that of the Hancock (MO) valve studied (PI = 0.41). The closure backflow for this valve design, 5.2 cm^3 /beat , was larger than that measured wuth the three porcine valves studied. This valve had the best leaflet opening and closing characteristics (opening area was 95% of stent orifice area) of the four tissue valves studied.

This valve design, like the previous two tissue valves, also produces a jet-like flow field. The jet is not axisymmertric, but skews towards the bottom of the flow channel. This is something that was not expected by examining the valve, since the valve appears to have a symmetric geometry. The skewness of the jet is probably due to the differeces in elestic characteristics of the three valve leaflets. The velocity of the jet has a maximum value of 231 cm/s at peak systole. The jet has a very steep velocity gradient which causes a drastic change in turbulent shear stress in the region around the jet. The turbulent shear stress could be as high as 2500 dynes/cm^2 , which could lead to sublethal and/or lethal blood element damage.

Flow separates from the downstream edge of the leaflets. Regions of flow separation are visible around

the jet and extend as far downstream as 80 cm from the valve sewing ring. The annular region between the outflow surfaces of the leaflets and the wall of the flow channel is stagnant. However, due to the convex shape of the leaflets, the region of stagnation is small, which should tend to reduce the possibility of calcific and thrombotic deposits, and tissue overgrowth. The highest estimated wall shear stress was about 400 dynes/cm^2 for this valve. The velocity profile upstream of the valve 20 ms after the end of systole, indicates a large amount of fluid is displaced by the closing movement of the valve leaflets, which creates negative velocities on the order of -35 cm/s.

(viii) Smeloff Caged Ball Valve*

The pressure drop characteristics of the Smeloff valve are better than the Starr-Edwards ball valve, but are still less than desirable. The Smeloff valve has a PI of 0.36. The regurgitation characteristics are quite baffling because of the excessive leakage flow that was measured (closing backflow 4.5 cm^3 /beat ; leakage backflow 11.6 cm^3 /beat)

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* Velocity measurements were not conducted with this valve.

This valve produces a circumferential jet-like flow field. The jet separates from the ball about 1/8th the way around it, with a 60 degree angle to the axial direction. A large turbulent wake can be observed distal to the ball throughout systole. This area of turbulence is caused by the vortices which are shed from the distal surface of the ball, as a result of boundary layer separation. The wake extends about 60 mm downstream of the sewing ring at peak systole.

The velocity of the fluid in the annular region between the ball and the flow channel wall appears to be very high and jet like. Since the poppet creates a lot of obstruction to the flow, the turbulent shear stresses produced by this valve design are also expected to be very high and quantitatively similar to those measured with the Starr-Edwards ball valve.

II . VALVES IN THE MITRAL POSITION

(i) Beall Caged-Disc Valve

The Beall caged disc valve was the most stenotic valve studied, with a performance index (PI) of 0.19. The valve is very stenotic even at a normal resting cardiac output. The valve had a closing back flow volume of 3.0 cm^3 /beat (@ 70 beats/min), and no measurable leakage volume during systole.

A very thin circumferential jet emerges around the valve occluder at peak systole with high velocity. The highest velocity measured was 113 cm/s. Flow separates from the edge of the occluder, which forms a large doughnut shaped vortex distal to the valve. Reverse flow occurs in the central part of the flow channel. A region of stagnation exists in the center of the flow field immediately adjacent to the downstream face of the occluder. Such a region of stagnation could lead to thrombus formation on the downstream face of the disc and the struts. This could lead to improper disc motion, and also increased disc wear. An annular region of flow separation exists adjacent to the downstream sewing ring, which could cause tissue overgrowth and/or thrombus formation around the sewing ring and the base of the struts.

This valve produces turbulent shear stress as high as 1900 dynes/cm^2 around the edge of the occluder, which could cause sublethal and/or lethal damage to blood elements. However, the high shear stress is confined to a thin region around the jet at peak flow, which decays very quickly as the flow travels downstream. The highest estimated wall shear stress for this valve design was 1780 dynes/cm^2 . Such wall shear stresses could damage the endothelial lining of the ventricular wall adjacent to the valve. The leakage back flow for this valve design is negligible.

(ii) Bjork-Shiley Convexo-Concave Tilting Disc Valve

In the mitral position the Bjork-Shiley valve had a PI of 0.38, which indicates that this valve design could be stenotic under severe exercise conditions. The closing back flow and leakage back flow volumes were 4.3 and 2.1 cm^3 /beat ,respectively.

The valve produces two jet type flow fields, one from the major orifice and the other from the minor orifice. The major orifice jet is wider than the minor orifice jet. Forward flow occurs mainly from the major orifice. The highest turbulent shear stress was measured in the major orifice jet and was on the order of 500 dynes/cm^2 . Such turbulent shear stresses could cause sublethal damage to

the blood elements. A small region upstream of the major orifice jet and adjacent to the downstream sewing ring, appears to be stagnant throughout entire diastole. This could lead to tissue overgrowth and/or thrombus formation along this region of the major orifice sewing ring. A large region of flow separation exists between the minor orifice jet and the flow channel wall. The region adjacent to the sewing ring in the minor orifice region is relatively stagnant, which makes it a possible site for tissue overgrowth. The region beneath the valve occluder in the minor orifice region is stagnant throughout the distole, which could lead to the deposition of thrombotic material on the outflow face of the disc.

The highest estimated wall shear stress was 620 dynes/cm^2 , and occurred approximately where the major orifice jet hit the wall of the flow channel. This magnitude of wall shear stress could cause sublethal damage to the endothelial lining of the ventricular wall. Small amounts of back flow exist adjacent to the flow channel wall, upstream of the valve. The highest turbulent shear stress caused by the leakage back flow was 80 dynes/cm^2 .

(iii) Medtronic-Hall Tilting Disc Valve

The Medtronic-Hall valve had relatively good pressure drop characteristics with a PI of 0.43. The closing and leakage back flow volumes were 4.7 and 2.4 cm^3 /beat , respectively. The regurgitation characteristics of this valve design could become clinically dignificant at low cardiac outputs (<3 l/min).

Most of the forward flow emerging from this valve is through the major orifice. The highest velocities are 105 cm/s and 97 cm/s in the major and the minor orifices, respectively. Turbulent shear stress as high as 2500 dynes/cm^2 were measured in the major orifice region immediately downstream of the strut superstructure. The highest turbulent shear stress measured in the minor orifice region was 1800 dynes/cm^2 . The occluder of the Medtronic-Hall mitral valve oscillates during diastole, which causes the flow field to be highly non-stationary. Such oscillations could lead to large fluctuations in the measured turbulent shear stresses, and cause an overall elevation of the turbulent shear field. The measured turbulent shear stress could cause sublethal and/or lethal damage to blood elements.

A vortex structure exists adjacent to the sewing ring in the major orifice region, between the jet and the flow channel wall. This vortex is caused by boundary layer

separation from the valve orifice ring. A large region of flow separation can be observed in the minor orifice region adjacent to the sewing ring and the strut. This region of flow separation could lead to tissue overgrowth and/or thrombus formation along the sewing ring and the strut in the minor orifice region. The highest estimated wall shear stress with this valve was 480 dynes/cm^2 , and occurred at the location where the major orifice jet hit the wall. Such wall shear stress could cause sublethal damage to the endothelial lining of the ventricular wall.

During systole, back flow occurs through the central pivot hole like a jet, with a velocity as high as -17 cm/s and turbulent shear stress as large as 700 dynes/cm^2 . This elevated shear stress could lead to blood cell damage.

(iv) St. Jude Bileaflet Valve

In the mitral position as well, the St. Jude bileaflet valve has the best pressure drop characteristics (PI = 0.48) of all the valve designed studies. Its regurgitation characteristics (closure volume 5.0 cm^3 /beat ; leakage volume 2.5 cm^3 /beat) could, however, cause clinical problems at low cardiac outputs.

The forward flow emerging form this valve is primarily through the two side orifices. At peak systole,

the valve produces three jet-like flow fields, two from the two side orifices and one form the center orifice. The peak velocities of the two side orifice jets are higher than that of the center orifice jet, with velocities as high as 103 cm/sec. The jets are centrally located in the flow channel, surrounded by an annular region of flow separation along the wall. The highest turbulent shear stress measured during diastole (760 dynes/cm^2) occurred in the center orifice flow field. This high shear stress occurs only at peak diastole and is confined to a narrow region. At this level of shear stress, blood cell damage may not be a serious problem. During our studies it had been observed that the two leaflets did not open synchronously, and the velocity measurements also confirmed this phenomenon, which is somewhat troubling.

The region of flow separation observed adjacent to the downstream sewing ring, especially in the vicinity of pivot mechanism, could lead to tissue overgrowth and/or thrombus formation, and interfere with the motion of the valve leaflets. The highest estimated wall shear stress during diastole was 200 dynes/cm^2 . During systole, back flow exists in the center part of the flow channel, with a reverse velocity as high as -17 cm/s, and a turbulent shear stress of 117 dynes/cm^2 .

(v) Hancock Standard Porcine Xenograft

The Hancock (Std) porcine valve is stenotic even at mild levels of excercise (PI = 0.26). The primary reason for this, is its poor leaflet motion characteristics. The valve leaflets opened to only 50% of the stent orifice area at a cardiac output of about 7.5 l/min.

This valve produces a high velocity central jet. The velocity of the jet is has a maximum value of 216 cm/s at peak diastole. Flow separates from the downstream edge of the valve leaflets creating a region of flow separation around the jet and extends about 30 mm downstream of the sewing ring. The separation region is not very disturbed. The annular region adjacent to the sewing ring is stagnant throughout entire diastole. This region of stagnation could lead to tissue overgrowth around the sewing ring, and encourage calcific, thrombotic and/or fibrotic deposits on the outflow faces of the leaflets.

The jet type flow creates high velocity gradients and also led to high turbulent shear stresses. The highest turbulent shear stress measured in the jet was 1947 dynes/cm^2 . Such high shear stress could lead to sublethal and/or lethal blood cell damage. The highest wall shear stress measured with this valve was 260 dynes/cm^2 . Leakage backflow with this valve design was negligible.

(vi) Ionescu-Shiley Pericardial Xenograft

In the mitral position the pressure drop characteristics of the Ionescu-Shiley were not impressive (PI = 0.32). At moderate levels of excercise the valve is stenotic. The valve leaflets opened to 79% of the stent orifice area at a cardiac output of 7.5 l/min. The closing back flow volume for this valve was 5.0 cm^3 /beat .

A high velocity jet-like flow also emerges from this valve, which occupied a narrow region in the central part of the flow channel. The highest velocity of the jet was 190 cm/sec. High turbulent shear stresses, up to 1400 dynes/cm^2 , exist in a thin region around the jet. Flow separates from the downstream edge of the valve leaflets. The region between the outflow surfaces of the valve leaflets and the wall of the flow channel is stagnant throughout diastole.

The high shear stresses created by this valve could lead to sublethal and/or lethal blood element damage. The region of stagnation around the valve leaflets could lead to tissue overgrowth around the sewing ring and encourage calcific, thrombotic and/or fibrotic deposits on the outflow surfaces of the leaflets. The highest estimated wall shear stress measured with this valve was 320 dynes/cm^2 . The measurements upstream of the valve during

systole showed that the back flow occurred in the center of the flow channel, which was caused by the closing movement of the valve leaflets.

CHAPTER 3

CONCLUSIONS AND RECCOMMENDATIONS

I CONCLUSIONS

Following the collection, analysis and interpretation of the *in vitro* fluid dynamic data, the following conclusion were made:

(i) The pressure drops studies revealed that the new low profile mechanical valves, such as the St. Jude and Medtronic-Hall, had the best pressure drop characteristics. The procine valves in current clinical use (Hancock and Carpentier-Edwards) had poor pressure drop characteristics which need to be improved *immediately* .

(ii) The low profile mecharical valves such as the Bjork-Shiley, St. Jude and Medtronic-hall prostheses have regurgitant volumes which could be clinically significant at low cardiac outputs.

(iii) All the valve designs (mechanical and tissue) studied created turbulent shear stresses large enough which could cause sublethal and/or lethal damage to blood elements. With the mechanical

valves, the elevated shear stresses were measured in the immediate vicinity of the valve superstructure. In the case of the tissue valves, the elevated turbulent shear stresses occurred in the bulk of the fluid.

(iv) Most of the valves studied in the aortic position created wall shear stresses which could cause subleathal and/or lethal damange to the endothelial lining of the aortic wall adjacent to the valve prosthesis.

(v) All of the valve protheses that were investigated, created regions of flow separation and/or stagnation adjacent to their respective superstructures, which could lead to tissue overgrowth, and thrombotic and/or calcific deposits.

(vi) The tissue valves studied (Hancock, Carpentier-Edwards and Ionescu-Shiley) have less than satisfactory leaflet motion characteristics. Of the tissue valves studied, the Ionescu-Shiley valve appeared to have the best in vitro fluid dynamic characteristics.

(vii) From an in vitro fluid dynamic point of view, none of the valves in current clinical use even approach ideal status . The lack of attention paid to subtle

design parameters is the major reason for most of the flaws in the current valve designs.

II RECOMMENDATIONS

(i) Further detailed *in vitro* regurgitation studies should be conducted with different designs of prosthetic heart valves, to investigate the effects of heart rate and cardiac output on regurgitant (ie: closure and leakage) volumes.

(ii) *In vivo* quantitative studies should also be conducted to evaluate the regurgitant characteristic of prosthetic heart valves.

(iii) Detailed studies should be performed on the pressure drop characteristics and the leaflet motion characteristics of all new trileaflet valve designs.

(iv) The pulsatile flow velocity measurments conducted in thes study should and must be expanded. Due to time and budget limitations experiments were only conducted at a normal resting cardiac output (5 to 6 l/min). It would be valuable to conduct similar studies at cardiac outputs of about 7.5 to 10 l/min to simulate excercise conditions.

(v) All prosthetic valve manufacturers should be required at a minimum to perform the following *in vitro* fluid dynamic studies:

(a) steady and pulsatile flow pressure drop measurements

(b) pulsatile flow regurgitation measurements

(c) pulsatile flow visualization

(d) leaflet motion studies (for leaflet valves only)

(vi) Detailed in vitro fluid dynamic studies should be conducted on selected recovered valve prostheses. Such studies must include pulsatile flow velocity and shear stress measurments.